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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Pamela Wingood Examiner #: 73103 Date: 3/14/03
Art Unit: 3736 Phone Number 301 2676 Serial Number: 091644, 676
Mail Box and Bldg/Room Location: CP2 4E14 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Xiaohong Peng

Earliest Priority Filing Date: 8/25/99 (?)

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

reagent for
ovulation / menstruation / period detection device

Claims 1, 7, 12 are similar.

Reagent is described by characteristics in these claims.

Check characteristics & also specifically named reagents chemicals for use as reagent in for ovul./etc. detection device.

STAFF USE ONLY

Type of Search

Vendors and cost where applicable

Searcher: <u>Jule Wilko</u>	NA Sequence (#)	STN
Searcher Phone #: <u>305-8587</u>	AA Sequence (#)	Dialog <input checked="" type="checkbox"/>
Searcher Location: <u>CP2-2008</u>	Structure (#)	Questel/Orbit
Date Searcher Picked Up: <u>3/14/03</u>	Bibliographic <input checked="" type="checkbox"/>	Dr.Link
Date Completed: <u>3/17/03</u>	Litigation	Lexis/Nexis
Searcher Prep & Review Time: <u>400 96m</u>	Fulltext <input checked="" type="checkbox"/>	Sequence Systems
Clerical Prep Time: _____	Patent Family	WWW/Internet <input checked="" type="checkbox"/>
Online Time: <u>50m 54m</u>	Other	Other (specify)

PTO-1590 (8-01)

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ovulation "Hydrogen peroxide" color

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Language: **English** -- Date: **Before August 1999** -- Block Offensive Content: **Never** [[Edit this Search](#)]

WEB RESULTS by Google (Showing Results 1 - 10 of 15)

1. Progesterone ELISA Test Kit

... are used to confirm whether **ovulation** has occurred ... with the peroxidase to produce **color** (blue) in ... 3' 5' 5'-tetramethylbenzidine (TMB) and **hydrogen peroxide** in a ...

<http://www.atlaslink-inc.com/elisa/progesterone.doc> - 0 B



2. Detection of Bromodeoxyuridine in Paraffin- embedded Tissue ...

... hydrochloride (DAB) and 0.02% **hydrogen peroxide** in TBS ... the cell nuclei stain a uniform blue with hematoxylin ... growth and atresia following **ovulation** in pigs ...

http://www.roche-applied-science.com/biochemica/no1_98/p17.pdf - 0 B

3. Effects of food deprivation . . .

... of reproduction including puberty, **ovulation**, reproductive behavior ... in the presence of **hydrog peroxide** (0.05%) and ... RECEPTORS 7 For digital (**color**) version in ...

http://www-unix.oit.umass.edu/~blaustei/YD_PRIRX.PDF - 0 B

4. Material Safety Data Sheet Dictionary

... Appearance includes the **color**, size, and consistency of a ... a structural derivative of **hydrogen peroxide** where one or ... **Ovulation** - The process in which an ovum is ...

<http://www.umd.edu/research/files/environ/appendic.htm> - 59 KB

5. Regulation of Cyclooxygenase Gene Expression in Rat Endometrial ...

... the cells were incubated in 0.1% **hydrogen peroxide** in PBS ... the cells was detected as a red c after incubation ... primarily due to a defect in **ovulation** and the ...

<http://publish.uwo.ca/~kennedyt/t109.pdf> - 0 B

6. untitled

... data for determining the time of **ovulation** in an ... Method and apparatus for multi-**color** laser e ... 423/700 5215735 Co-production of **hydrogen peroxide** and a ...

<http://ftp.std.com/obi/Patents/Titles/930601> - 101 KB

7. INDEX OF DIETARY SUPPLEMENTS

... An experiment with **hydrogen peroxide**-induced cytotoxicity and ... bees and gives her incredibl stamina, **ovulation** ability and ... but may range in **color** from black to ...

<http://vitamindigest.bestnutrition.com/dietary-supplements.htm> - 81 KB

8. untitled

... catalase: enzyme that breaks down **hydrogen peroxide**. ... produced by the epidermis that gives **color**. ... **ovulation**: in human females, the monthly release of an ...

<http://www.geocities.com/SunsetStrip/Palladium/9613/lifesci.htm> - 61 KB

9. Herb Information From A Contributor's Files

... First wash out the ears with warmed **Hydrogen Peroxide**, I use a ... 30 seconds she sat up and t **color** returned to ... usually 1/4 to 1/2 tsp starting after **ovulation**. ...

<http://www.gentlebirth.org/archives/herbsvol.html> - 101 KB

10. untitled

... ble so that changes in the **color** of the ... 1. Medications such as, salt, **hydrogen peroxide** (3%)
... the later stages of menopause when **ovulation** has nearly ...
<http://www.icomm.ca/survival/medic90.don/30-medic.htm> - 101 KB

« Previous | Next »

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Set	Items	Description
S1	4875	OVULAT? OR LUTEINIZ? OR LUTEINIS?
S2	31871	HYDROGEN() PEROXIDE OR H2O2
S3	274554	COLOR? OR COLOUR?
S4	244602	BENZIDINE OR TETRAMETHYLBENZIDINE OR DIAMINOBENZIDINE OR S- ALT? ? OR 3()AMINO()9()ETHYLCARBAZOLE OR 4()METHOXY(2W)NAPHTH- OL OR O() (TOLIDINE OR DIANISIDINE OR METHOXYPHENOL OR PHENYLE- NEDIAMINE) OR 5()AMINOSALICYLIC OR PYROGALLOL
S5	392	S1 AND S2 AND (S3 OR S4)
S6	125	S5 AND IC=(A61B OR G01N)
S7	9966	S2(S) (S3 OR S4)
S8	68	S7 AND S1 AND IC=(A61B OR G01N)
S9	68	IDPAT (sorted in duplicate/non-duplicate order)
S10	65	IDPAT (primary/non-duplicate records only)

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File 348:EUROPEAN PATENTS 1978-2003/Mar W02

(c) 2003 European Patent Office

File 349:PCT FULLTEXT 1979-2002/UB=20030306,UT=20030227

(c) 2003 WIPO/Univentio

bibli NPL

8/5/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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05335228 EMBASE No: 1993103313

Semiquantitative assay of human chorionic gonadotropin by a simple and fast immunofiltration technique

Rapak A.; Szewczuk A.

European Journal of Clinical Chemistry and Clinical Biochemistry (EUR. J. CLIN. CHEM. CLIN. BIOCHEM.) (Germany) 1993, 31/3 (153-157)

CODEN: EJCBE ISSN: 0939-4974

An immunofiltration technique for the semiquantitative assay of human chorionic gonadotropin (hCG) was applied in two versions, using different antibodies. One anti-betahCG subunit was immobilized on a glass microfibre disc in the form of six radially located bars, and the dry disc was placed on a water-absorbing material in a plastic device. A second antibody labelled with horse radish peroxidase conjugate was used in solution. For the **colour** reaction a solution with **tetramethylbenzidine** and **hydrogen peroxide** was used. The number of blue bars appearing on the test disc depended on concentration range of human chorionic gonadotropin. The technique with the monoclonal antibodies, anti-betahCG and anti-alphahCG-horse radish peroxidase conjugate, was specific for intact human chorionic gonadotropin, while the technique with the rabbit antibodies, raised against synthetic fragment 122-145-betahCG and betahCG-horse radish peroxidase, was useful for both intact human chorionic gonadotropin and its beta-chain. Cross reactions with human lutropin and thyrotropin were negligible. Haemoglobin, urea and various tested drugs did not affect the assay. In the assay of human chorionic gonadotropin in the urine of pregnant women and in sera of patients with trophoblastic diseases, the results from the immunofiltration technique were in accordance with data obtained by classical ELISA and by two commercial kits.

8/5/9 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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04383808 JICST ACCESSION NUMBER: 99A0930603 FILE SEGMENT: JICST-E
Ovulation and Trace Elements.

SASAKI JUNZO (1); KIMURA TOJI (1); KOGAMI TAKASHI (1); MIKI YUKARI (1);
NOMURA TAKAKO (1); SHINOHARA ATSUKO (2); CHIBA MOMOKO (2)

Biomed Res Trace Elem, 1999, VOL.10,NO.1, PAGE.25-31, FIG.2, TBL.3, REF.18
JOURNAL NUMBER: L1046AAS ISSN NO: 0916-717X

LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan

ABSTRACT: The expression of Mn-SOD mRNA during PMSG/hCG-induced **ovulation** and the estrous cycle in rat female reproductive organs was investigated by in situ hybridization. Before **ovulation** occurred, expression was observed in the theca interna cells. Just after **ovulation** had occurred, expression became marked in granulosa cells exhibiting **luteinization**, and later expression was localized in the corpora lutea. Expression of Mn-SOD mRNA was not induced in granulosa cells of unovulated follicles. Various elements in the ovary during PMSG/hCG- **ovulation** were analyzed by atomic absorption spectrometry, **colorimetry** or microwave-induced plasma mass-spetrometry(MIP-MS). The treatment with PMSG increased the ovary weight from 0.0098g to 0.0149g,

and further treatment with hCG increased it to 0.0202g. Five elements were found to be present in large amounts in the following order; K>P>Na>Mg>Ca. The weight-s of these elements increased with increase in the ovary weight. Marked increases in weight of Mn, Cu, Zn, Rb, Fe and Se were also observed. Laloraya and colleagues have suggested that LH-induced SOD might generate **hydrogen peroxide**, so enhancing the peroxidase-ascorbate system responsible for the production of progesterone from pregnenolone. In the present study, the expression of Mn-SOD mRNA in the ovary began in cells that initiated the synthesis of progesterone. The marked expression of Mn-SOD mRNA observed in the adrenal cortex supports the above hypothesis. Progesterone itself has been reported to be involved in the **ovulation** process. LH-induced Mn-SOD may determine the **ovulating** follicles by triggering progesterone synthesis. The role of SODs as scavenger enzymes has been emphasized in oxygen radical studies. On the other hand, the above results suggest that Mn-SOD or reactive oxygen species are involved in cellular metabolism including steroidogenesis in the ovaries. (author abst.)

8/5/10 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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06070653 89160888 PMID: 3231643

The development of over-the-counter (OTC) assays for pregnanediol-3-glucuronide and estrone-B,D-glucuronide.

Bahar I

Progress in clinical and biological research (UNITED STATES) 1988, 285 p139-51, ISSN 0361-7742 Journal Code: 7605701

The development of simple tests for estrone-B,D-glucuronide (E1G) and pregnanediol-3-glucuronide (P3G) in urine is described. The haptens P3G and E1G, coupled to bovine serum albumin (BSA), were used as immunogens against which specific monoclonal antibodies were made by fusion of variants of P3.X63.Ag8.653 with spleen lymphocytes from immunized mice. When covalently bonded to gelatin or BSA and passively adsorbed to a microtiter plate, the hapten provides the solid phase for an ELISA. Peroxidase-labelled monoclonal antibody is premixed with a urine specimen and the mixture is immediately added to the plate. After a brief incubation and washing, a mixture of **tetramethylbenzidine** chromogen and **hydrogen peroxide** is added to serve as substrate and generate **color**. The ELISA can be used to monitor levels of E1G and P3G during menstrual cycles and provides a simple, noninvasive method which can be used in a laboratory. A similar competitive assay can be performed using colloidal gold as the label instead of peroxidase. The replacement of peroxidase by colloidal gold further simplifies the procedure and could be used as the basis for an OTC test.

8/5/11 (Item 2 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

04558661 84241345 PMID: 6376666

[Study on the new development of highly sensitive E2-EIA used by two specific binding systems and on the clinical application]

Terada N; Shirotake S; Maekawa I; Kobori T; Takamizawa H

Languages: JAPANESE

As a tracer, biotin was bound to the amino group of newly synthesized 6-ethylenediamino-17-beta-estradiol. Two competitive methods were developed by using the tracer (E2-B). Method I, E2-B, sample, and anti E2 antibody conjugated with horse radish peroxidase were mixed, and the mixture was added to the avidin immobilized on a microplate to separate free and bound tracer. Then the enzyme activity which remained after washing was measured by using **H2O2** and **o - phenylenediamine**. E2 was quantified from 75 pg/ml to 9.6 ng/ml; (II) E2-B and the samples were added to the anti E2 adsorbed on a microplate. After washing, the avidin conjugated with HRP was put into the immune complex plate, and the enzyme activity which remained was determined to calculate E2. The standard curve indicated E2 from 75 pg/ml to 19.2 ng/ml. The E2 values obtained by the new methods correlated with those by 3H-RIA and the EIA was useful in monitoring the induction of ovulation .

8/TI/1 (Item 1 from file: 5)
DIALOG(R)File 5:(c) 2003 BIOSIS. All rts. reserv.

CYTOCHEMICAL DETECTION OF RECEPTORS SPECIFIC FOR N-LINKED OLIGOSACCHARIDES
OF GLYCOPROTEINS IN THE MEMBRANE OF THE HUMAN SPERMATOZOON AND THEIR
DISTRIBUTION IN THE DIFFERENT ZONES OF THAT MEMBRANE

8/TI/2 (Item 2 from file: 5)
DIALOG(R)File 5:(c) 2003 BIOSIS. All rts. reserv.

QUANTITATIVE IMMUNOCYTOCHEMISTRY OF HYPOTHALAMIC AND PITUITARY HORMONES
VALIDATION OF AN AUTOMATED COMPUTERIZED IMAGE ANALYSIS SYSTEM

8/TI/3 (Item 3 from file: 5)
DIALOG(R)File 5:(c) 2003 BIOSIS. All rts. reserv.

ENZYMATIC OXIDATION OF ACETYL TRYPTOPHANAMIDE AND TRYPTOPHAN CONTAINING
PEPTIDES FORMATION OF DEHYDRO TRYPTOPHAN

8/TI/4 (Item 4 from file: 5)
DIALOG(R)File 5:(c) 2003 BIOSIS. All rts. reserv.

SIMULTANEOUS VISUALIZATION BY LIGHT MICROSCOPY OF 2 PITUITARY HORMONES IN A
SINGLE TISSUE SECTION USING A COMBINATION OF INDIRECT IMMUNO
HISTOCHEMICAL METHODS

8/TI/5 (Item 1 from file: 34)
DIALOG(R)File 34:(c) 2003 Inst for Sci Info. All rts. reserv.

Title: DEVELOPMENT OF A SIMPLE, RAPID SANDWICH ENZYME-IMMUNOASSAY FOR THE
MEASUREMENT OF SERUM RAT LH

8/TI/6 (Item 2 from file: 34)
DIALOG(R)File 34:(c) 2003 Inst for Sci Info. All rts. reserv.

Title: EFFECTS OF INERT FAT ON ENERGY-BALANCE, PLASMA-CONCENTRATIONS OF
HORMONES, AND REPRODUCTION IN DAIRY-COWS

8/TI/8 (Item 2 from file: 73)
DIALOG(R)File 73:(c) 2003 Elsevier Science B.V. All rts. reserv.

Direct enzyme immunoassay of estradiol in serum of women enrolled in an
in vitro fertilization and embryo transfer program

Set	Items	Description
S1	279678	OVULAT? OR LUTEINIZ? OR LUTEINIS?
S2	221127	HYDROGEN() PEROXIDE OR H2O2
S3	1343839	COLOR? OR COLOUR?
S4	1157698	BENZIDINE OR TETRAMETHYLBENZIDINE OR DIAMINOBENZIDINE OR S-ALT? ? OR 3()AMINO()9()ETHYLCARBAZOLE OR 4()METHOXY(2W)NAPHTH-OL OR O() (TOLIDINE OR DIANISIDINE OR METHOXYPHENOL OR PHENYLE-NEDIAMINE) OR 5()AMINOSALICYLIC OR PYROGALLOL
S5	16	S1 AND S2 AND (S3 OR S4)
S6	11	RD (unique items)
S7	11	S6 NOT PY>1999
S8	11	S7 NOT PD>19990825

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File 2:INSPEC 1969-2003/Mar W2
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File 34:SciSearch(R) Cited Ref Sci 1990-2003/Mar W2
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File 35:Dissertation Abs Online 1861-2003/Feb
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File 65:Inside Conferences 1993-2003/Mar W2
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File 73:EMBASE 1974-2003/Mar W2
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File 94:JICST-EPlus 1985-2003/Mar W3
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File 144:Pascal 1973-2003/Mar W2
(c) 2003 INIST/CNRS

File 155:MEDLINE(R) 1966-2003/Mar W2
(c) format only 2003 The Dialog Corp.

File 172:EMBASE Alert 2003/Mar W3
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File 198:Health Devices Alerts(R) 1977-2003/Mar W3
(c) 2003 ECRI-nonprft agncy

File 399:CA SEARCH(R) 1967-2003/UD=13812
(c) 2003 American Chemical Society

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info

File 48:SPORTDiscus 1962-2003/Mar
(c) 2003 Sport Information Resource Centre

File 71:ELSEVIER BIOBASE 1994-2003/Mar W3
(c) 2003 Elsevier Science B.V.

File 91:MANTIS(TM) 1880-2002/Oct
2002 (c) Action Potential

File 162:CAB Health 1983-2003/Jan
(c) 2003 CAB International

File 164:Allied & Complementary Medicine 1984-2003/Mar
(c) 2003 BLHCIS

File 467:ExtraMED(tm) 2000/Dec
(c) 2001 Informania Ltd.

*Inventor
Search*

4/5/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2003 Thomson Derwent. All rts. reserv.

014073823

WPI Acc No: 2001-558036/200163

XRAM Acc No: C01-166067

XRPX Acc No: N01-414722

Ovulation test reagent box for natural method contraception -

NoAbstract

Patent Assignee: PENG X (PENG-I)

Inventor: **PENG X**

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1152713	A	19970625	CN 95115790	A	19951024	200163 B

Priority Applications (No Type Date): CN 95115790 A 19951024

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

CN 1152713 A G01N-033/52

Title Terms: **OVULATION** ; TEST; REAGENT; BOX; NATURAL; METHOD;
CONTRACEPTIVE; NOABSTRACT

Derwent Class: B04; P31; S03; T01

International Patent Class (Main): G01N-033/52

International Patent Class (Additional): A61B-010/00; G06C-003/00

File Segment: CPI; EPI; EngPI

4/5/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2003 Thomson Derwent. All rts. reserv.

013663767

WPI Acc No: 2001-147979/200116

XRPX Acc No: N01-108401

**Heat-insulating and water-proofing integrated roofing structure of
building and its construction method**

Patent Assignee: ZHANG Z (ZHAN-I)

Inventor: MING S; **PENG X**; ZHANG Z

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1272580	A	20001108	CN 99117875	A	19990917	200116 B

Priority Applications (No Type Date): CN 99117875 A 19990917

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

CN 1272580 A E04D-011/02

Abstract (Basic): CN 1272580 A

NOVELTY - The present invention relates to a roofing structure integrating heat-insulating layer and water-proofing layer into one whole and its construction method. In particular, it is an energy-saving flat roof formed from roof boarding, sloping layer, heat-insulating (vapour barrier and water-proofing) layer and protective layer. The main technique of construction is characterized by laying and adhering heat-insulating layer, firstly the PE board is laid and adhered from one end and from upper portion to lower portion

to form a whole body, if the roofing has the organized drainage, the parapet skirting and drain and vent water-proofing can be made. Said roofing structure is simple in structure, convenient for construction, energy can be saved by 50% and water-proofing **period** can be up to above 50 years.

DwgNo 0/0

Title Terms: HEAT; INSULATE; WATER; PROOF; INTEGRATE; ROOF; STRUCTURE;
BUILD; CONSTRUCTION; METHOD

Derwent Class: Q45

International Patent Class (Main): E04D-011/02

File Segment: EngPI

4/5/3 (Item 3 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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013430676

WPI Acc No: 2000-602619/200058

XRAM Acc No: C00-180415

Method of bacteria culture preservation

Patent Assignee: BEIJING SANITARY & ANTIEPIDEMIC STATION (BEIJ-N)

Inventor: LU W; **PENG X**; WU J

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1142535	A	19970212	CN 96105227	A	19960521	200058 B

Priority Applications (No Type Date): CN 96105227 A 19960521

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
CN 1142535	A		C12N-001/20	

Abstract (Basic): CN 1142535 A

NOVELTY - A method for storing bacterial strain includes such steps as rolling special cotton ball to take cultured bacterial strain's lawn on it, quickly putting it in treated small tube, and immediately putting the tube in refrigerator at -20 to -30degreesC. Its storage **period** is two years.

DwgNo 0/0

Title Terms: METHOD; BACTERIA; CULTURE; PRESERVE

Derwent Class: B04; D16

International Patent Class (Main): C12N-001/20

International Patent Class (Additional): C12M-001/24; C12M-001/26

File Segment: CPI

4/5/4 (Item 4 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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013194582

WPI Acc No: 2000-366455/200032

XRAM Acc No: C00-110871

XRPX Acc No: N00-274100

Ovulation -testing reagent kit for natural contraception - comprise **first reagent comprising benzidines compound and stabilizer, and second reagent comprising hydrogen peroxide solution, swab and measuring glass**

Patent Assignee: PENG X (PENG-I)

Inventor: **PENG X**

Number of Countries: 094 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1247900	A	20000322	CN 99118909	A	19990825	200032 B
WO 200113799	A1	20010301	WO 2000CN226	A	20000808	200114
AU 200062581	A	20010319	AU 200062581	A	20000808	200136

Priority Applications (No Type Date): CN 99118909 A 19990825 ✓

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
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CN 1247900	A			C12Q-001/28	
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WO 200113799	A1	C		A61B-010/00	
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Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA
CH CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200062581	A			A61B-010/00	Based on patent WO 200113799
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Abstract (Basic): CN 1247900 A

The reagent kit consists of reagent A comprising 1-10%
concentration benzidines compound and stabilizer, reagent B of 1-10%
concentration hydrogen peroxide solution, swab and measuring glass.

ADVANTAGE - convenient, fast, accurate and stable, it is used in
testing **ovulation period** of women for natural contraception and is
also suitable for testing **ovulation period** of mammal.

Title Terms: **OVULATION** ; TEST; REAGENT; KIT; NATURAL; CONTRACEPTIVE;
COMPRISE; FIRST; REAGENT; COMPRISE; COMPOUND; SECOND; REAGENT; COMPRISE;
HYDROGEN; PEROXIDE; SOLUTION; SWAB; MEASURE; GLASS

Derwent Class: B04; D16; P31

International Patent Class (Main): A61B-010/00; C12Q-001/28

International Patent Class (Additional): C12N-001/28; G01N-033/50

File Segment: CPI; EngPI

4/5/5 (Item 5 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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012599567

WPI Acc No: 1999-405671/199935

XRAM Acc No: C99-119968

**Process for preparing bactericide containing silver - includes stirring
aqueous solution and adding acid to it**

Patent Assignee: JIANG H (JIAN-I)

Inventor: JIANG C; JIANG H; **PENG X**

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1214867	A	19990428	CN 97108681	A	19971021	199935 B

Priority Applications (No Type Date): CN 97108681 A 19971021

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
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CN 1214867	A			1 A01N-059/16	
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Abstract (Basic): CN 1214867 A

The preparation of silver-contained bactericide includes: using
silver oxide as raw material, adding distilled water, stirring and
dropping concentrated acid into it, when its pH is 2 - 3.5, taking

clear liquor and adding hydrogen peroxide so as to obtain the bactericide containing silver ion. Said invention is a simple process, has short production **period**, is higher in the valence state and concentration of the silver ion contained in the bactericide, strong in bactericidal action and extensive in application range.

Dwg.0

Title Terms: PROCESS; PREPARATION; BACTERIA; CONTAIN; SILVER; STIR; AQUEOUS
; SOLUTION; ADD; ACID
Derwent Class: D22; E32
International Patent Class (Main): A01N-059/16
File Segment: CPI

4/5/6 (Item 6 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2003 Thomson Derwent. All rts. reserv.

012399426

WPI Acc No: 1999-205533/199918

XRAM Acc No: C99-060048

XRPX Acc No: N99-151394

Vacuum packaging method for desulfurizing agent - for hydrogen sulfide, thiocarbon oxide and carbon disulfide at atmosphere temperature

Patent Assignee: HUBEI CHEM INST (HUBE-N)

Inventor: **PENG X**; WANG G; WANG X

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1201746	A	19981216	CN 98113487	A	19980330	199918 B

Priority Applications (No Type Date): CN 98113487 A 19980330

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
CN 1201746	A	1	B65B-031/02	

Abstract (Basic): CN 1201746 A

A vacuum packing method for ordinary-temp desulfurizing agent of H₂S, COS, or CS₂ includes such steps as loading the desulfurizing agent into package, pumping out air contained in the package and pores of desulfurizing agent, and filling N₂ or CO₂, methane, or argon to make the desulfurizing agent protected by inertial gas. Its advantage is long storage **period** without performance reduction.

Dwg.0/0

Title Terms: VACUUM; PACKAGE; METHOD; AGENT; HYDROGEN; OXIDE; CARBON; ATMOSPHERE; TEMPERATURE

Derwent Class: E36; J01; Q31; Q34

International Patent Class (Main): B65B-031/02

International Patent Class (Additional): B65D-081/20

File Segment: CPI; EngPI

4/5/7 (Item 7 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2003 Thomson Derwent. All rts. reserv.

011480452

WPI Acc No: 1997-458357/199743

XRAM Acc No: C97-146474

Delicious pickled vegetable liquid

Patent Assignee: PENG X (PENG-I)

Inventor: **PENG X**

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1118662	A	19960320	CN 94111730	A	19940511	199743 B

Priority Applications (No Type Date): CN 94111730 A 19940511

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
CN 1118662	A		A23L-001/218	

Abstract (Basic): CN 1118662 A

The pickled vegetable liquid comprises edible salt, sugar, gourmet powder, sodium pyrophosphate, potassium sorbate, lactic acid and water. It is suitable for soaking vegetables. The pickled vegetables are crisp, tender and convenient to use, do not become mildewed and have a long preservation period .

Title Terms: PICKLE; VEGETABLE; LIQUID

Derwent Class: D13

International Patent Class (Main): A23L-001/218

File Segment: CPI

4/5/8 (Item 8 from file: 350)

DIALOG(R)File 350:Derwent WPIX

(c) 2003 Thomson Derwent. All rts. reserv.

011471588

WPI Acc No: 1997-449495/199742

XRAM Acc No: C97-143480

XRPX Acc No: N97-374456

Stable serial Fullerene negative ion quaternary ammonium salt compound preparation

Patent Assignee: UNIV JILIN (UYJI-N)

Inventor: LI L; **PENG X** ; ZHANG Y

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1117092	A	19960221	CN 94109381	A	19940819	199742 B

Priority Applications (No Type Date): CN 94109381 A 19940819

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
CN 1117092	A	11	C25B-003/04	

Abstract (Basic): CN 1117092 A

The compound is prepared by an electrochemical reduction process, using a cationic semi-permeable film as the electrolyser diaphragm to reduce fullerene molecules in organic solvent. A quaternary ammonium salt is used as the reactant material to obtain fullerene negative ion quaternary ammonium salt compound. The supporting electrolyte may be the same quaternary ammonium salt or other conventional electrolyte. Through column chromatographic separation and the reduced pressure distillation in a water bath, a black solid product is obtained.

ADVANTAGE - The compound is stable in air and water for a long period .

Dwg.0/1

Title Terms: STABILISED; SERIAL; NEGATIVE; ION; QUATERNARY; AMMONIUM; SALT; COMPOUND; PREPARATION

Derwent Class: E19; J03; L02; X25

International Patent Class (Main): C25B-003/04

File Segment: CPI; EPI

4/5/9 (Item 9 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2003 Thomson Derwent. All rts. reserv.

011168257

WPI Acc No: 1997-146182/199714

XRAM Acc No: C97-046751

Growth controlling agent for water melon

Patent Assignee: PENG X (PENG-I)

Inventor: **PENG X** ; WEI K

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CN 1090710	A	19940817	CN 94100295	A	19940112	199714 B

Priority Applications (No Type Date): CN 94100295 A 19940112

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
CN 1090710	A	1	A01N-065/00	

Abstract (Basic): CN 1090710 A

A growth controlling agent for water melon is prepd. by decocting 18 Chinese-medicinal herbs e.g. herba verbenae officinalis, xanthium fruit, pinellia tuber and astragalus root, filtering to remove residue, adding wheat grains, decocting, concentrating and adding of the juice from another herb. The agent has a long acting **period**, controls vine growing and increases the quantity and quality of water melon.

Title Terms: GROWTH; CONTROL; AGENT; WATER; MELON

Derwent Class: C03

International Patent Class (Main): A01N-065/00

File Segment: CPI

4/5/10 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2003 European Patent Office. All rts. reserv.

01270655

OVULATION DETECTING AGENTS AND THE USE THEREOF
AGENTS DE DETECTION DE L' OVULATION ET LEUR UTILISATION
PATENT ASSIGNEE:

Peng, Xiahong, (3262460), Suite 102, No. 60, Changxin Flat, Xin District, Wuxi City, Jiangsu Province 214028, (CN), (Applicant designated States: all)

INVENTOR:

Peng, Xiahong, Suite 102, No. 60, Changxin Flat, Xin District, Wuxi City, Jiangsu Province 214028, (CN)

PATENT (CC, No, Kind, Date):

WO 2001013799 010301

APPLICATION (CC, No, Date): EP 2000949047 000808; WO 2000CN226 000808

PRIORITY (CC, No, Date): CN 99118909 990825

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI

INTERNATIONAL PATENT CLASS: A61B-010/00; G01N-033/50; C12N-001/28

CITED PATENTS (WO A): WO 8002596 A ; WO 9221774 A ; FR 2652092 A ; CN 1150178 A ; CN 1152713 A ; US 4614715 A

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application: 010425 A1 International application. (Art. 158(1))
Application: 010425 A1 International application entering European
phase
Application: 021023 A1 International application. (Art. 158(1))
Appl Changed: 021023 A1 International application not entering European
phase
Withdrawal: 021023 A1 Date application deemed withdrawn: 20020326
LANGUAGE (Publication,Procedural,Application): English; English;

Set	Items	Description
S1	141	E3,E5,E9
S2	11	S1 AND (OVULAT? OR PERIOD? OR MENSTRUAT?)
S3	11	IDPAT (sorted in duplicate/non-duplicate order)
S4	10	IDPAT (primary/non-duplicate records only)

? show files

File 347:JAPIO Oct 1976-2002/Nov(Updated 030306)
(c) 2003 JPO & JAPIO

File 348:EUROPEAN PATENTS 1978-2003/Mar W02
(c) 2003 European Patent Office

File 349:PCT FULLTEXT 1979-2002/UB=20030306,UT=20030227
(c) 2003 WIPO/Univentio

File 350:Derwent WPIX 1963-2003/UD,UM &UP=200317
(c) 2003 Thomson Derwent

File 371:French Patents 1961-2002/BOPI 200209
(c) 2002 INPI. All rts. reserv.

8/3,K/3 (Item 3 from file: 442)
DIALOG(R)File 442:AMA Journals
(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

00046720
Copyright (C) 1989 American Medical Association

Reactivity of Epidermal Growth Factor Receptor Monoclonal Antibodies With Human Uterine Tissues (ORIGINAL ARTICLE)

BERCHUCK, ANDREW; SOISSON, ANDREW P.; SOPER, JOHN T.; CLARKE-PEARSON, DANIEL L.; BAST, ROBERT C.; MCCARTY, KENNETH S.
Archives of Pathology and Laboratory Medicine
October, 1989 ; 113: 1155-11581989;

... 1 hour and then incubated for 10 minutes in phosphate-buffered saline with 0.3% **hydrogen peroxide** to neutralize endogenous peroxidase. The slides were fixed in acetone for 10 minutes at room...

... followed by the avidin-peroxidase complex. Finally, the slides were developed with the enzyme substrate **diaminobenzidine** (5 mg/mL) and 0.03% **hydrogen peroxide**. Tissue sections were counterstained with hematoxylin and mounted (Crystal Mount, Lerner Laboratories, Pittsburgh, Pa).

Immunohistochemical...

...was no relationship between menstrual phase and reactivity with MAB 29.1 among the 15 **ovulatory** patients.

Staining was seen in 19 of 20 uterine tissue samples using MAB 528 (Figure...

... bottom right, is not easily discernible in this black-and-white photomicrograph. Among the 15 **ovulatory** patients in this study, 8 were in the proliferative (follicular) phase and 7 were in...

... patients were all found to stain in a similar fashion to those from the 14 **ovulatory** patients in which staining was seen.

COMMENT

Peptide growth factors and their cell membrane receptors...

8/3,K/4 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals
(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

00043073
Copyright (C) 1988 American Medical Association

Human Chorionic Gonadotropin Expression in Lung, Breast, and Renal Carcinomas (ORIGINAL ARTICLE)

KUIDA, CHRISTINE A.; BRAUNSTEIN, GLENN D.; SHINTAKU, PETER; SAID, JONATHAN W.
Archives of Pathology and Laboratory Medicine
March, 1988; 112: 282-2851988;

...to tap water. Endogenous peroxidase activity was blocked by treating the slides with fresh 3% **hydrogen peroxide** in absolute methanol for 15

minutes. Following tap water washing, the tissues were treated with...

... National Hormone and Pituitary Program, National Institutes of Health, Bethesda, Md) and 39 ng of **luteinizing** hormone/follicle-stimulating hormone (LER 907, National Institutes of Health). Following incubation and rinsing, biotinylated...

... antiperoxidase (Dako) was used for the PAP series. Following additional incubation and rinsing, 0.05% **diaminobenzidine** , 0.03% **hydrogen peroxide** was added to the tissues for five minutes following rinsing in PBS and tap water...method, theoretically, has a greater sensitivity over the PAP method due to amplification of the **color** signal by large complexes of avidin-biotin-horseradish peroxidase and reduced potential for nonspecific immunoglobulin...

CITED REFERENCES:

...Pathol 1985;84:687-696.

15. Jagiello G, Mesa-Tejada R: Cross-reactivity of human **luteinizing** hormone (beta-subunit) and a serine protease demonstrated by immunoperoxidase staining in human oocytes. Endocrinology...

8/3,K/6 (Item 6 from file: 442)

DIALOG(R)File 442:AMA Journals

(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

00036795

Copyright (C) 1983 American Medical Association

New Developments in Immunoperoxidase Techniques and Their Application (SPECIAL ARTICLE)

FALINI, BRUNANGELO

Archives of Pathology and Laboratory Medicine

March, 1983; 107: 105-117/1983;

... techniques use either horseradish peroxidase with different substrate-chromogen systems (Ref. 3) to produce contrasting **colors** , or different enzymes (horseradish peroxidase, alkaline phosphatase, glucose oxidase) with their corresponding distinctively **colored** reaction products. (Ref. 41-44) These methods have some advantages over analogous "double immunofluorescence techniques...

...antibodies is dissociated (Ref. 3,45,46) (after development of the first peroxidase reaction with **hydrogen peroxide** and the chromogen) without removing the **colored** peroxidase reaction product (brown with **diaminobenzidine** tetrahydrochloride). The staining procedure is then repeated with a primary antibody of different specificity, followed...

... and another chromogen, usually 4-chloro-1-naphthol, resulting in a reaction product of different **color** . More recently, Sternberger (Ref. 47) found that two antigens may be identified in the same...xylol-

... or surface antigens present in different cellular populations but, by the formation of a mixed, **colored** reaction, also permit ... immunostaining. For example, Joseph and Sternberger (Ref. 135,136) demonstrated that adrenocorticotrophic hormone and beta- **luteinizing** hormone are located in the same pars intermedia cells of the pituitary and

are probably...in endogenous peroxidase, particularly when the usual method for blocking endogenous peroxidase activity (methyl alcohol- **hydrogen peroxide**) cannot be used because of its adverse effects on some cell surface antigens. (Ref. 145...

CITED REFERENCES:

...Masson Publications USA Inc, 1980, vol 1, pp 15-49.

8/TI/1 (Item 1 from file: 442)
DIALOG(R)File 442:(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

Herbal Remedies in Psychiatric Practice (ARTICLE)

8/TI/2 (Item 2 from file: 442)
DIALOG(R)File 442:(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

Histologic and Immunohistochemical Evidence for Considering Ovarian Myxoma as a Variant of the Thecoma-Fibroma Group of Ovarian Stromal Tumors (ARTICLE)

8/TI/5 (Item 5 from file: 442)
DIALOG(R)File 442:(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

Immunohistochemical Localization of Chromogranin in Human Hypophyses and Pituitary Adenomas (ORIGINAL ARTICLE)

8/TI/7 (Item 7 from file: 442)
DIALOG(R)File 442:(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

Immunohistochemical Localization of Neuron-Specific Enolase in the Human Hypophysis and Pituitary Adenomas (ORIGINAL ARTICLE)

8/TI/8 (Item 8 from file: 442)
DIALOG(R)File 442:(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.

Cellular Immunity to Sperm in Infertile Women (ORIGINAL CONTRIBUTIONS)

8/TI/9 (Item 1 from file: 444)
DIALOG(R)File 444:(c) 2003 Mass. Med. Soc. All rts. reserv.

An Aromatase-Producing Sex-Cord Tumor Resulting In Prepubertal Gynecomastia (Brief Report)

8/TI/10 (Item 2 from file: 444)
DIALOG(R)File 444:(c) 2003 Mass. Med. Soc. All rts. reserv.

Clinical and Pathological Features and Laboratory Confirmation of Creutzfeldt-Jakob Disease in a Recipient of Pituitary-Derived Human Growth Hormone (Medical Intelligence)

8/TI/11 (Item 1 from file: 98)
DIALOG(R)File 98:(c) 2003 The HW Wilson Co. All rts. reserv.

Effect of neonatal exposure to estrogenic compounds on development of the excurrent ducts of the rat testis through puberty to adulthood.

8/TI/12 (Item 1 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.

Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina.

8/TI/13 (Item 2 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.

Neural tube defects in embryos of diabetic mice: role of the Pax-3 gene and apoptosis.

8/TI/14 (Item 3 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.

A practical approach to hirsutism. (includes patient information sheet)

8/TI/15 (Item 4 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.

Pulsatile insulin secretion from isolated human pancreatic islets.

8/TI/16 (Item 5 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.

Autocrine or paracrine inflammatory actions of corticotropin-releasing hormone in vivo.

8/TI/17 (Item 6 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.

Your role in radiation therapy.

Set	Items	Description
S1	4954	OVULAT? OR LUTEINIZ? OR LUTEINIS?
S2	6561	HYDROGEN() PEROXIDE OR H2O2
S3	99842	COLOR? OR COLOUR?
S4	42602	BENZIDINE OR TETRAMETHYLBENZIDINE OR DIAMINOBENZIDINE OR S- ALT? ? OR 3()AMINO()9()ETHYLCARBAZOLE OR 4()METHOXY(2W)NAPHTH- OL OR O() (TOLIDINE OR DIANISIDINE OR METHOXYPHENOL OR PHENYLE- NEDIAMINE) OR 5()AMINOSALICYLIC OR PYROGALLOL
S5	20	S1 AND S2 AND (S3 OR S4)
S6	19	RD (unique items)
S7	18	S6 NOT PY>1999
S8	17	S7 NOT PD>19990825

? show files

File 441:ESPICOM Pharm&Med DEVICE NEWS 2003/Mar W2

(c) 2003 ESPICOM Bus.Intell.

File 442:AMA Journals 1982-2003/Jun B3

(c)2003 Amer Med Assn -FARS/DARS apply

File 444:New England Journal of Med. 1985-2003/Mar W3

(c) 2003 Mass. Med. Soc.

File 95:TEME-Technology & Management 1989-2003/Feb W4

(c) 2003 FIZ TECHNIK

File 98:General Sci Abs/Full-Text 1984-2003/Feb

(c) 2003 The HW Wilson Co.

File 135:NewsRx Weekly Reports 1995-2003/Mar W1

(c) 2003 NewsRx

File 149:TGG Health&Wellness DB(SM) 1976-2003/Mar W1

(c) 2003 The Gale Group

File 369:New Scientist 1994-2003/Mar W1

(c) 2003 Reed Business Information Ltd.

File 370:Science 1996-1999/Jul W3

(c) 1999 AAAS

FT Patents

10/5,K/12 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2003 European Patent Office. All rts. reserv.

00503080

TOTAL GONADOTROPAL ALPHA PEPTIDE CHAIN ASSAY

NACHWEISVERFAHREN FUR DEN TOTALGEHALT AN GONADOTROPEN ALPHA-PEPTIDKETTEN

DOSAGE DE LA TENEUR TOTALE EN CHAINES PEPTIDIQUES ALPHA GONADOTROPES

PATENT ASSIGNEE:

Hygeia Sciences, Inc., (822650), 330 Nevada Street, Newton Massachusetts
02160-1432, (US), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

INVENTOR:

CLOUGH, Kathleen, M., 36 Spruce Street, Acton, MA 01720, (US)
COLE, Francis, X., 75 Kirkland Drive, Stow, MA 01775, (US)

LEGAL REPRESENTATIVE:

Bizley, Richard Edward et al (28352), Hepworth, Lawrence, Bryer & Bizley
Merlin House Falconry Court Baker's Lane, Epping Essex CM16 5DQ, (GB)
PATENT (CC, No, Kind, Date): EP 537154 A1 930421 (Basic)

EP 537154 A1 931118

EP 537154 B1 960605

WO 9115594 911017

APPLICATION (CC, No, Date): EP 91907306 910329; WO 91US2121 910329

PRIORITY (CC, No, Date): US 505307 900405

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: C12Q-001/00; G01N-033/76 ; G01N-033/543

CITED PATENTS (EP A): US 4196123 A; WO 8304312 A

CITED REFERENCES (EP A):

BIOLOGICAL ABSTRACTS vol. 88, no. 11 , 1989, Philadelphia, PA, US;
abstract no. 118277, M. S. BALIN ET AL. 'Evaluation of the human
gonadotroph free alpha-subunit secretory pools by administration of
gonadotropin hormone-releasing hormone into normal subjects at
different phases of the ovarian cycle.' page AB-338 ;

BIOLOGICAL ABSTRACTS vol. 88, no. 5 , 1989, Philadelphia, PA, US;
abstract no. 48241, C. RIVIER ET AL. 'Immunoneutralization of
endogenous inhibin modifies hormone secretion and ovulation rate in the
rat.' page AB-337 ;;

NOTE:

No A-document published by EPO

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application: 930421 A1 Published application (A1with Search Report
;A2without Search Report)

Examination: 930421 A1 Date of filing of request for examination:
921028

Change: 931110 A1 Obligatory supplementary classification
(change)

Search Report: 931118 A1 Drawing up of a supplementary European search
report: 930929

Examination: 950208 A1 Date of despatch of first examination report:
941222

Grant: 960605 B1 Granted patent

*Assignee: 960710 B1 Proprietor of the patent (transfer of rights):
Hygeia Sciences, Inc. (822651) c/o
Carter-Wallace, Inc., 1345 Avenue of the
Americas New York, New York 10105 (US)
(applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

*Assignee: 960710 B1 Previous applicant in case of transfer of rights (change): Hygeia Sciences, Inc. (822650)
330 Nevada Street Newton Massachusetts
02160-1432 (US) (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

Oppn None: 970528 B1 No opposition filed
LANGUAGE (Publication,Procedural,Application): English; English; English

...SPECIFICATION in mammalian body fluids and in particular to assays for determining and/or detecting the **luteinizing** hormone surge which results in rupture of the preovulatory follicle and release of the ovum at **ovulation** . More particularly, the invention relates to the use of total gonadotrophal alpha peptide chain content in urine as an enhanced indicator of **luteinizing** hormone content. Even more particularly, the invention relates to an immunoassay suitable for testing for...

...discovered that the traditional mid cycle surge of intact LH in the system that triggers **ovulation** is accompanied by a contemporaneous surge in the total level of gonadotrophal alpha peptide chains...using two solutions. The first, TMB solution, is prepared by adding 4.75 g of **tetramethylbenzidine** to 3.8 L of methanol. This solution should be protected from light. The second...

...75.27 g sodium phosphate dibasic, 0.31 g sodium stannate, 5.2 mL 30% **hydrogen peroxide** and 0.26 g thimerosal in sufficient purified water to bring the total volume to...

10/5,K/17 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2003 European Patent Office. All rts. reserv.

00387812

Reagent for immunoassay, and device using the same.
Reagenz fur Immuntestverfahren und Gerat zur Verwendung davon.
Reactif d'essai immunologique et dispositif a cet effet.

PATENT ASSIGNEE:

MOCHIDA PHARMACEUTICAL CO., LTD., (469262), 7, Yotsuya 1-chome,
Shinjuku-ku Tokyo 160, (JP), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

INVENTOR:

Sato, Hiroshi, 3-201, 3-1-1, Sakurada, Washimiya-cho, Kitakatsushika-gun,
Saitama, (JP)

Yamauchi, Tadakazu, 2-10-16, Hon-cho, Kawaguchi-shi, Saitama, (JP)

Izako, Toshio, 23-1, Kitami 4-chome, Setagaya-ku Tokyo, (JP)

Nobuhara, Masahiro, 572-10, Yajuro Koshigaya-shi, Saitama, (JP)

Mochida, Ei, 5-4, Komagome 2-chome, Toshima-ku Tokyo, (JP)

LEGAL REPRESENTATIVE:

Henkel, Feiler, Hanzel & Partner (100401), Mohlstrasse 37, D-8000 Munchen
80, (DE)

PATENT (CC, No, Kind, Date): EP 383313 A2 900822 (Basic)
EP 383313 A3 921125

APPLICATION (CC, No, Date): EP 90102909 900214;

PRIORITY (CC, No, Date): JP 8935815 890215

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: G01N-033/74 ; G01N-033/557 ; G01N-033/58 ;

G01N-033/574 ; G01N-033/543 ; G01N-033/76 ; G01N-033/532

CITED PATENTS (EP A): EP 88974 A

CITED REFERENCES (EP A):

PATENT ABSTRACTS OF JAPAN vol. 11, no. 378 (P-645)(2825) 10 December 1987

PATENT ABSTRACTS OF JAPAN vol. 11, no. 386 (P-647)(2833) 17 December 1987

;

ABSTRACT EP 383313 A2

A reagent for use in an immunoassay for measuring haptens, antigens or antibodies by means of a competitive binding method, which comprises a combination of an antibody and a labelled hapten or a labelled antigen or a combination of a hapten or an antigen and a labelled antibody, wherein the antibody and the labelled hapten or the labelled antigen in one combination or the hapten or the antigen and the labelled antibody in another combination are capable of undergoing reversible binding, and a device for use in an immunoassay wherein the reagent of the present invention is included in a single container.

An immunoassay can be performed in a short time by the use of the immunoassay device of the present invention.

ABSTRACT WORD COUNT: 126

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application: 900822 A2 Published application (Alwith Search Report ;A2without Search Report)

Search Report: 921125 A3 Separate publication of the European or International search report

Examination: 930331 A2 Date of filing of request for examination: 930121

Examination: 940727 A2 Date of despatch of first examination report: 940610

Refusal: 961002 A2 Date on which the European patent application was refused: 960513

LANGUAGE (Publication,Procedural,Application): English; English; English

...SPECIFICATION the present invention can also be used for the measurement of antigens, such as a **luteinizing** hormone (LH), a thyroid-stimulating hormone (TSH), a human chronic gonadotropin (hCG) and a carcinoembryonic ...to a monitor system of the female gonadal functions, especially maturation of ovarian follicles and **ovulation** .

The antibody for use in the measurement of estradiol may be obtained by immunizing an...process. Thereafter, the enzyme (peroxidase) reaction was performed for 10 minutes in the presence of **hydrogen peroxide** as the substrate and orthophenylenediamine as the **color** reagent and then the absorbance of the **colored** solution was measured.

The solution containing the peroxidase-labelled estrogen derivative was added to another...process. Thereafter, the enzyme (peroxidase) reaction was performed for 10 minutes in the presence of **hydrogen peroxide** as the substrate and orthophenylenediamine as the **color** reagent and then the absorbance of the **colored** substance was measured.

To another glass tube in which the purified monoclonal anti-estradiol antibody...

10/5,K/21 (Item 21 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

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00335217

Positive step immunoassay.

Schwellwertimmunoassay.

Essai immunologique a seuil defini.

PATENT ASSIGNEE:

Hygeia Sciences, Inc., (822650), 330 Nevada Street, Newton Massachusetts
02160-1432, (US), (applicant designated states:

BE;DE;ES;FR;GB;IT;NL;SE)

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PATENT (CC, No, Kind, Date): EP 327843 A1 890816 (Basic)
EP 327843 B1 930818

APPLICATION (CC, No, Date): EP 89100758 890118;

PRIORITY (CC, No, Date): US 153081 880208

DESIGNATED STATES: BE; DE; ES; FR; GB; IT; NL; SE

INTERNATIONAL PATENT CLASS: G01N-033/53 ; G01N-033/74 ; G01N-033/553

CITED PATENTS (EP A): EP 114614 A; CA 1183080 A; GB 2029011 A; EP 86095 A;
EP 158746 A

ABSTRACT EP 327843 A1

An assay procedure that is particularly valuable for detecting and/or determining the presence of threshold levels of analyte ligands in biological fluids. In one particularized and specialized aspect the disclosure is directed to procedures for detecting and/or determining threshold levels of hormone metabolites such as pregnanediol-3-glucuronide (P(sub 3)G) and estrone-3-glucuronide (E(sub 1)3G) in human urine. The assay consists of contacting a sample containing the analyte with a known amount of an antibody thereto and with a calibrated amount of the analyte itself that is conjugated to said solid support. When the level of the analyte in the sample exceeds a threshold level, such as 5 ug/ml for P(sub 3)G, the antibody will be insufficient to block all of the corresponding analyte on the solid support. Thus, upon addition of labelled antibody to the assay system, a detectable immunoreaction product becomes attached to the support to indicate that the amount of analyte in the sample exceeds the threshold level. On the other hand, if the level of the analyte in the sample is below the threshold amount, the free antibody will be sufficient to block all of the corresponding analyte on the solid support preventing labelled antibody from forming a detectable immunoreaction product on the support and thus no signal will appear.

ABSTRACT WORD COUNT: 215

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application: 890816 A1 Published application (A1with Search Report
;A2without Search Report)

Change: 900328 A1 Representative (change)

Examination: 900411 A1 Date of filing of request for examination:
900212

Examination: 920408 A1 Date of despatch of first examination report:
920225

Grant: 930818 B1 Granted patent

Oppn None: 940810 B1 No opposition filed

LANGUAGE (Publication,Procedural,Application): English; English; English

...SPECIFICATION detecting the presence of threshold levels of hormones such as progestin and estrogen derivatives and **luteinizing** hormone (LH) in human urine samples. The invention also relates to kits of materials for...hormones from the female glands and organs. Such release is predictable and specifically related to **ovulation** by which ova are released from the ovaries and the lining of the uterus is...

...E(sub 1)3G) in female urine begins to rise about 6 days prior to **ovulation** and reaches its peak about 1 day before **ovulation** and falls rapidly during and after **ovulation**. The level of pregnanediol-3-glucuronide (P(sub 3)G) in female urine begins to rise on the day of **ovulation**, and reaches a peak 2 to 3 days after **ovulation** and remains elevated for the duration of the luteal phase. Likewise, the relationship between P...

...amount of P(sub 3)G in urine would be extremely valuable in determining whether **ovulation** has occurred.

The positive step immunoassay procedure of the present invention addresses each of the...the liquid sample (for example, the threshold level of P(sub 3)G indicating that **ovulation** has occurred) and no signal at a lower level. Since the physiological detection of P...to make sure that all non-specifically bound HRP is removed. 50 ul of a **color** developing substrate solution comprising a fresh mixture of 3 ml. of 0.125% **tetramethylbenzidine** in methanol and 7 ml. of 0.03% **hydrogen peroxide** in a 0.1 M phosphate and 50 mM citric acid aqueous solution (pH 5 allowed to react for 5 minutes at room temperature. The intensity of the **color** formation was read on a Dynatech plate reader (Dynatech, Virginia) at 630 nm with a...and E(sub 1)3G assays of the present invention may be used to predict **ovulation** in advance, verify **ovulation**, assess luteal function, detect the beginning and end of the fertile period assess follicular phase to measure the increase in P(sub 3)G in FMU during **ovulation** and during the luteal phase and can be calibrated to provide a positive color indication...

10/5,K/23 (Item 23 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00271578

Monoclonal antibodies.
Monoklonale Antikörper.
Anticorps monoclonaux.

PATENT ASSIGNEE:

Bunge (Australia) Proprietary Limited, (789581), 6th Floor 616 St. Kilda Road, Melbourne Victoria 3004, (AU), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)

INVENTOR:

Mountford, Peter Scott, 45 Waterloo Crescent, St. Kilda Victoria, (AU)

LEGAL REPRESENTATIVE:

Harding, Richard Patrick et al, Arthur R. Davies & Co. 27 Imperial Square, Cheltenham GL50 1RQ, (GB)

PATENT (CC, No, Kind, Date): EP 265156 A2 880427 (Basic)
EP 265156 A3 900829

APPLICATION (CC, No, Date): EP 87309057 871014;

PRIORITY (CC, No, Date): AU 868482 861014; AU 869525 861216

DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: C12P-021/00; C12N-015/00; C12N-005/00;

G01N-033/577 ; G01N-033/76 ; A61K-037/24; A61K-039/395; A61K-049/00
CITED PATENTS (EP A): US 4565687 A; EP 151030 A; EP 107551 A

ABSTRACT EP 265156 A2

A monoclonal antibody against equine chorionic gonadotrophin produced from a continuous cell line which produces a monoclonal antibody against equine chorionic gonadotrophin, including a hybridoma formed by fusion of a B cell capable of producing antibodies against equine chorionic gonadotrophin with a myeloma cell and its use in purifying equine chorionic gonadotrophin and modifying the biological activity of equine chorionic gonadotrophin.

ABSTRACT WORD COUNT: 64

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application: 880427 A2 Published application (A1with Search Report
;A2without Search Report)
Search Report: 900829 A3 Separate publication of the European or
International search report
Examination: 910109 A2 Date of filing of request for examination:
901113
Examination: 910821 A2 Date of despatch of first examination report:
910704
Withdrawal: 940126 A2 Date on which the European patent application
was deemed to be withdrawn: 930803

LANGUAGE (Publication,Procedural,Application): English; English; English

...SPECIFICATION hCG).

eCG has a potent, dual LH-FSH bioactivity capable of inducing follicular growth and **ovulation** when injected into a wide range of domestic animals. The hormone has a particularly long...

...This may be given before antibody administration and about 24 hours before the time of **ovulation**.

The use of monoclonal antibodies for controlling eCG in vivo whether for use in superovulation...sup ,)-diaminobenzidine tetrachloride in 250ml 0.01M citrate buffer, pH 5, plus 250ul of 30% **hydrogen peroxide** added immediately prior to use. Within 10 minutes the reaction was stopped by rinsing in...ewes is also accompanied by a rise in the numbers of corpora lutea and therefore **ovulations**.

The use of the monoclonal antibody has increased the **ovulation** rate and reduced the number of undesirable large follicles.

EXAMPLE 5

Five doses of a...

10/5,K/29 (Item 29 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2003 European Patent Office. All rts. reserv.

00235526

IMMUNOASSAY METHOD AND KIT.

IMMUNTESTVERFAHREN UND SATZ.

KIT ET PROCEDE D'ANALYSE IMMUNOLOGIQUE.

PATENT ASSIGNEE:

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PATENT (CC, No, Kind, Date): EP 238631 A1 870930 (Basic)

EP 238631 A1 890809

EP 238631 B1 930317

WO 8701811 870326

APPLICATION (CC, No, Date): EP 86906108 860919; WO 86US1944 860919

PRIORITY (CC, No, Date): US 778554 850920

DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: G01N-033/535 ; G01N-033/547 ; G01N-033/74

CITED PATENTS (EP A): DE 2736684 A

CITED PATENTS (WO A): US 3888629 A; US 4280816 A; US 4517288 A; WO 8505451
A

CITED REFERENCES (EP A):

See also references of WO8701811;

CITED REFERENCES (WO A):

The Journal of Biological Chemistry, Vol. 255, No. 2, issued January 25,
1980 (WILLIAMS & WILKINS Co., Baltimore, Md 212202), E.O'KEEFE et al.,
"Use of Immunoglobulin-Loaded Protein A...", pages 561-568, see page
562, column 1, Lines 11-28; page 563, column 1, Lines 1-13, 23-28; page
568 column 1, Lines 24-28.

IDEM

The Journal of Laboratory and Clinical Medicine, Vol. 98, No. 1, issued
July 1981, (C.V. MOSBY Co., St. Louis, MO. 63141), J. JUNGERS et al. "A
Simple and Rapid Radioimmunoassay...", pages 30-36, see Abstract.

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(WILLIAMS & WILKINS Co., Baltimore, Md 21202) S.W. KESSLER, "Cell
Membrane Antigen Isolation...", pages 1482-1490, see page 1483, column
1, Lines 10-30.

The Lancet, Vol. 1 for 1985, issued January 5, 1985 (London, WC2N 6AD
England) R.J. NORMAN et al., "Dipstick Method for Human Chorionic
Gonadotropin...", pages 19-20, see page 19, column 2, Lines 31-38.

Clinical Chemistry, Vol. 31, No. 9, issued September 1985 (Winston-Salem,
NC 27107) G.E. VALKIRS et al, "Immunoconcentration- A New Format for
Solid-Phase Immunoassays", pages 1427-1431, see Abstract; page 1427,
column 2, Lines 4-23;

NOTE:

No A-document published by EPO

LEGAL STATUS (Type, Pub Date, Kind, Text):

Lapse: 20000209 B1 Date of lapse of European Patent in a
contracting state (Country, date): AT
19930317, BE 19930317, CH 19930317, LI
19930317, LU 19930930, NL 19930317, SE
19930317,

Application: 870930 A1 Published application (A1with Search Report
;A2without Search Report)

Examination: 870930 A1 Date of filing of request for examination:
870526

Search Report: 890809 A1 Drawing up of a supplementary European search
report: 890621

Change: 900404 A1 Representative (change)
Examination: 910220 A1 Date of despatch of first examination report:
901227
Grant: 930317 B1 Granted patent
Lapse: 931110 B1 Date of lapse of the European patent in a
Contracting State: CH 930317, LI 930317, NL
930317
Lapse: 931110 B1 Date of lapse of the European patent in a
Contracting State: CH 930317, LI 930317, NL
930317
Lapse: 931110 B1 Date of lapse of the European patent in a
Contracting State: CH 930317, LI 930317, NL
930317
Lapse: 931118 B1 Date of lapse of the European patent in a
Contracting State: CH 930317, LI 930317, NL
930317, SE 930317
Lapse: 931124 B1 Date of lapse of the European patent in a
Contracting State: BE 930317, CH 930317, LI
930317, NL 930317, SE 930317
Oppn None: 940309 B1 No opposition filed
Lapse: 940622 B1 Date of lapse of the European patent in a
Contracting State: AT 930317, BE 930317, CH
930317, LI 930317, NL 930317, SE 930317
LANGUAGE (Publication,Procedural,Application): English; English; English

...SPECIFICATION the placenta during pregnancy.

The lowest progesterone level in animals corresponds to estrus (time of **ovulation**) and the highest progesterone level occurs near the midpoint of a normal ovarian cycle.

During...benzidine (TMB) (2 mmol/(liters)) and nicotinamide adenine dinucleotide (NADH) (0.4 mmol/(liters)) with **hydrogen peroxide** (2 mmol/(liters)) was added to develop the test **color** and these results illustrated in Figure 6.

No background color occurs at the high progesterone...

10/5,K/33 (Item 33 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00917432

SELENO-CYSTEINE CONTAINING PROTEIN ZSEL1
PROTEINE ZSEL1 CONTENANT DE LA SELENOCYSTEINE

Patent Applicant/Assignee:

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, US, US (Residence), US (Nationality)

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Legal Representative:

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200250274 A2 20020627 (WO 0250274)

Application: WO 2001US48769 20011212 (PCT/WO US0148769)

Priority Application: US 2000256685 20001218

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU

*Bad
Date*

CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO
RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: C12N-015/12

International Patent Class: C07K-014/46; C07K-016/18; C12Q-001/68;

G01N-033/53

Publication Language: English

Filing Language: English

English Abstract

Novel zsell polypeptides, polynucleotides encoding the polypeptides, and related compositions and methods are disclosed. Also disclosed are antibodies to the zsell protein or fragments thereof.

Legal Status (Type, Date, Text)

Publication 20020627 A2 Without international search report and to be republished upon receipt of that report.

...International Patent Class: **G01N-033/53**

Fulltext Availability:

Detailed Description

Detailed Description

... Sigma)) I.P. to induce superovulation. Donors are mated with studs subsequent to hormone injections. **Ovulation** generally occurs within 13 hours of hCG injection.

Copulation is confirmed by the presence of...detection antibody can be horseradish peroxidase, a commonly used enzyme that acts upon the substrate **hydrogen peroxide**. The reduction of peroxide by the enzyme is achieved by hydrogen donors that can be measured after oxidation as a **color** change.

Commonly used chemicals for this are O-phenylene diamine (OPD) and tetrarnethlybenzidine (TMB...

10/5,K/36 (Item 36 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00864156

NUCLEOTIDE AND AMINO ACID SEQUENCES OF OOCYTE FACTORS FOR ALTERING OVARIAN FOLLICULAR GROWTH IN VIVO OR IN VITRO

Patent Applicant/Assignee:

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(Residence), NZ (Nationality), (For all designated states except: US)

Patent Applicant/Inventor:

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RITVOS Olli Visa-Pekka, Visakoivuntie 10 G 13, FIN-02130 Espoo, FI, FI (Residence), FI (Nationality)

DAVIS George Henry, Invermay Agricultural Centre, Private Bag 50034, Mosgiel, Dunedin, NZ, NZ (Residence), NZ (Nationality), (Designated

*B^{ad}
Date*

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MCNATTY Kenneth Pattrick, Wallaceville Animal Research Centre, P.O. Box
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only for: US)
VUOJOLAINEN Kaisa Niina Johanna, Koskelantie 23 H 67, FIN-00610 Helsinki,
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Legal Representative:
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Patent and Priority Information (Country, Number, Date):
Patent: WO 200196393 A2-A3 20011220 (WO 0196393)
Application: WO 2001NZ113 20010615 (PCT/WO NZ0100113)
Priority Application: NZ 502796 20000615
Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU
CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class: C07K-014/51
International Patent Class: A61P-015/08; C12N-015/12; C12N-015/00;
C12N-005/10; A61K-038/18; C07K-016/22; A61K-048/00; A01K-067/027;
G01N-033/74
Publication Language: English
Filing Language: English

English Abstract

The present invention relates to nucleotide and amino acid sequences of oocyte factors for altering ovarian follicular growth in vivo or in vitro. The present invention also concerns novel homodimeric and heterodimeric polypeptides and their use for altering mammalian ovarian follicular growth in vivo or in vitro. In particular, the invention broadly concerns active or passive immunisation against these homo- or heterodimeric polypeptides or functional fragments or variants thereof so as to alter follicular growth in vivo or in vitro.

Legal Status (Type, Date, Text)

Publication 20011220 A2 Without international search report and to be
republished upon receipt of that report.
Search Rpt 20020808 Late publication of international search report
Republication 20020808 A3 With international search report.
Search Rpt 20020808 Late publication of international search report
Correction 20021128 Corrected version of Pamphlet: page 24, sequence
listing, added
Republication 20021128 A3 With international search report.
Examination 20030227 Request for preliminary examination prior to end of
19th month from priority date

Detailed Description

... antral follicles) has been poorly understood. On the other hand,

follicle-stimulating hormone (FSH) and **luteinising** hormone are glycoprotein hormones derived from the pituitary and have generally been accepted as the...

...the single most important factor for stimulating a greater than normal number of follicles to **ovulate**, a fact that is well illustrated by the wide use of commercial FSH preparations in...

...added for 1 h at 37'C. The wells were then washed and developed with **o - phenylenediamine** plus **hydrogen peroxide** with development being stopped with sulphuric acid.

The ewes were each given 100 ml of...

10/5,K/43 (Item 43 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00805310 **Image available**

DEVICES AND METHODS FOR DETECTING ANALYTES USING ELECTROSENSOR HAVING CAPTURE REAGENT

Patent Applicant/Assignee:

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Inventor(s):

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Legal Representative:

CHEN Peng (et al) (agent), Morrison & Foerster LLP, Suite 500, 3811 Valley Centre Drive, San Diego, CA 92130-2332, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200138873 A2-A3 20010531 (WO 0138873)

Application: WO 2000US29748 20001027 (PCT/WO US0029748)

Priority Application: US 99167409 19991124

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ

DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ

LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG

SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: **G01N-033/543**

Publication Language: English

Filing Language: English

English Abstract

The present invention relates to devices comprising electrosensors containing capture reagents, their preparation thereof, and their use for detecting preferably, quantitative measurement, of analyte in a liquid sample. In particular, the invention relates to an enzyme electrosensor, e.g., electroimmunosensor, device for electrochemical detection and preferably, real-time measurement, which is suitable for use at point-of-care settings by unskilled personnel.

Legal Status (Type, Date, Text)

Bad Date

Publication 20010531 A2 Without international search report and to be
republished upon receipt of that report.
Examination 20010920 Request for preliminary examination prior to end of
19th month from priority date
Search Rpt 20020711 Late publication of international search report
Republication 20020711 A3 With international search report.

Detailed Description

... used for detection of pregnancy, strep throat, and bacteria, as well as for prediction of **ovulation**. Examples of such assays are described in U.S. Patent Nos. 5,622,871, 4703...a label, when other necessary current-generating component(s) is provided. For example, horseradish peroxidase, **hydrogen peroxide** and at least one electron transfer mediator(s), such as ferrocene, or a derivative thereof, benzoquinone, ascorbic acid or 3, 3', 5, 5' **tetramethylbenzidine**, are needed to generate electrocurrent. Any one or two, but not all three, of the horseradish peroxidase, **hydrogen peroxide** and electron transfer mediator can be used as such a label(s).

As used herein...used. In a specific embodiment, the enzyme is horseradish peroxidase and the enzymatic substrate is **hydrogen peroxide** and the electron transfer mediator is ferrocene, or a derivative thereof, benzoquinone, ascorbic acid or 3, 3', 5, 5' **tetramethylbenzidine**.

The device can further comprise a cover casing having a liquid sample application aperture and...be used. In a specific embodiment, the enzyme is horseradish idase and the enzymatic substrate **hydrogen peroxide** and the electron peroxi transfer mediator is ferrocene, or a derivative thereof, benzoquinone, ascorbic acid or 3, 3', 5, 5' **tetramethylbenzidine**.

The sample application area must be in fluid communication with the electrosensor. Preferably, the...O.IM sodium acetate (pH 6.0) solution containing 5-10% dimethylsulfoxide, and 0.01% **hydrogen peroxide** as a co-substrate for HRP enzymatic reaction.

Alternatively, ready-to-use liquid substrate solution containing TMB, buffer, and **hydrogen peroxide** can be obtained from commercial sources. Examples of such ready-touse substrate solutions include K...

10/5,K/44 (Item 44 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00469584 **Image available**

MEMBER OF THE TNF FAMILY USEFUL FOR TREATMENT AND DIAGNOSIS OF DISEASE
MEMBRE DE LA FAMILLE DU FACTEUR DE NECROSE TUMORALE (TNF) UTILE POUR LE
TRAITEMENT ET LE DIAGNOSTIC DE MALADIES

Patent Applicant/Assignee:

ABBOTT LABORATORIES,

Inventor(s):

WILEY Steven R,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9900518 A1 19990107

Application: WO 98US12101 19980612 (PCT/WO US9812101)

Priority Application: US 97883086 19970626

Designated States: CA JP MX AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL
PT SE

Main International Patent Class: C12Q-001/68
International Patent Class: C07K-014/525; C07K-016/22; C12N-015/63;
C12N-015/28; C12N-005/10; A61K-031/70; **G01N-033/50 ; G01N-033/68**
Publication Language: English

English Abstract

An isolated clone consisting of sequences transcribed from the TNF-gamma gene. Also provided are human polypeptides translated from said TNF-gamma sequences and a procedure for producing such polypeptide by recombinant techniques. Also provided are a procedure for producing soluble biologically active TNF-gamma, which may be used to treat deficiencies of TNF-gamma and diseases conditions ameliorated by TNF-gamma. Antibodies, antagonists and inhibitors of such polypeptide which may be used to prevent the action of such polypeptide and therefore may be used therapeutically to treat TNF-gamma associated diseases, tumors or metastases are disclosed. Also disclosed is the use of said antibodies, agonists and inhibitors as well as the nucleic acid sequences to screen for, diagnose, prognosticate, stage and monitor conditions and diseases attributable to TNF-gamma, especially inflammation. The use of said partial sequence to provide antibodies, agonists and inhibitors as well as partial nucleic acid sequences to screen for, diagnose, stage and monitor diseases associated with TNF-gamma, including but not limited to inflammation. Illustrative sequences and clone designations for TNF-gamma are provided.

Detailed Description

... hypertrophic scars, i.e. keloids. Another use is as a birth control agent, by inhibiting **ovulation** and establishment of the placenta. TNF-gamma is also useful in the treatment of diseases...wells to 100 pL of ABTS solution (2,2'-azinobis-[3-ethylbenzothiazoline sulfonic acid] diammonium **salt**) (Pierce Chemical Co., Rockford, IL, USA). Alternatively, **color** development can be achieved with the addition to each well of 100 pL of a solution of phenylene diamine (OPD) in **hydrogen peroxide**, and a 10 n-dn incubation

10/5,K/47 (Item 47 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00444597

MEMBER OF THE TNF FAMILY USEFUL FOR TREATMENT AND DIAGNOSIS OF DISEASE
ELEMENT DE LA FAMILLE TNF UTILISE POUR LE TRAITEMENT ET LE DIAGNOSTIC D'UNE
MALADIE

Patent Applicant/Assignee:

ABBOTT LABORATORIES,

Inventor(s):

WILEY Steven R,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9835061 A2 19980813

Application: WO 98US2859 19980212 (PCT/WO US9802859)

Priority Application: US 97798692 19970212; US 9821706 19980210

Designated States: CA JP MX AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT
SE

Main International Patent Class: C12Q-001/68

International Patent Class: C12N-15:63; C07K-14:525; C07K-16:28;
G01N-33:50 ; G01N-33:574 ; A61K-38:19

Publication Language: English

English Abstract

An isolated clone comprising sequences transcribed from the TREPA gene. Also provided are human polypeptides translated from said TREPA sequences and a procedure for producing such polypeptide by recombinant techniques. Also provided are a procedure for producing soluble biologically active TREPA, which may be used to treat deficiencies of TREPA and diseases conditions ameliorated by TREPA. Antibodies, antagonists and inhibitors of such polypeptide which may be used to prevent the action of such polypeptide and therefore may be used therapeutically to treat TREPA-associated diseases, tumors or metastasies are disclosed. Also disclosed is the use of said antibodies, agonists and inhibitors as well as the nucleic acid sequences to screen for, diagnose, prognosticate, stage and monitor conditions and diseases attributable to TREPA, especially inflammation. The use of said partial sequence to provide antibodies, agonists and inhibitors as well as partial nucleic acid sequences to screen for, diagnose, stage and monitor diseases associated with TREPA, including but not limited to inflammation. Illustrative sequences and clone designations for TREPA are provided.

Detailed Description

... hypertrophic scars, i.e. keloids. Another use is as a birth control agent, by inhibiting **ovulation** and establishment of the placenta. TREPA is also useful in the treatment of diseases that...wells to 100 @iL of ABTS solution (2,21-azinobis-[3-ethylbenzothizoline sulfonic acid] diammonium **salt**) (Pierce Chemical Co., Rockford, IL, USA). Alternatively, **color** development can be achieved with the addition to each well of 100 pl of a solution of o-phenylene diamine (OPD) in **hydrogen peroxide** and a 10 min incubation at room temperature. The **color** development reaction is quenched with 100 4l of 1N sulfuric acid. The **colors** in the wells are read as absorbance with a Dynatech MR5000 plate reader at 490...

10/5,K/55 (Item 55 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2003 WIPO/Univentio. All rts. reserv.

00204813

GEL PHASE TRANSITION CONTROLLED BY INTERACTION WITH A STIMULUS
TRANSITION DE PHASE D'UN GEL COMMANDEE PAR L'INTERACTION D'UN STIMULUS

Patent Applicant/Assignee:

MASSACHUSETTS INSTITUTE OF TECHNOLOGY,
Inventor(s):

TANAKA Toyoichi,
KOKUFUTA Etsuo,
ZHANG Yong-Quing,
SUZUKI Atsushi,
MAMADA Akira,
HIROKAWA Yoshitsugu,
TOKITA Masayuki,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9202005 A2 19920206
Application: WO 91US5312 19910726 (PCT/WO US9105312)
Priority Application: US 90733 19900726

Designated States: AT BE CA CH DE DK ES FR GB GR IT JP LU NL SE

Publication Language: English

English Abstract

A phase-transition gel and a method of forming a phase-transition gel which undergoes a significant discontinuous volume change at a desired phase-transition condition in response to a stimulus is disclosed. The phase transition gel includes a liquid medium gelled with a polymer network which has a phase transition condition different from that desired and a phase-transition-modifying agent sufficient to cause, in response to the stimulus, the discontinuous volume change of the gel at the desired phase-transition condition.

Claim

... esterase, urease, amylase, lipase, galactosidase, catalase, protease, etc, Examples of substrates include sugars, lipids, proteins, **hydrogen peroxide**, etc* it is to be understood that an enzyme inhibitor can be used to interact...

...the gel, thereby causing the phase transition. An example of a suitable chromophore is trisodium **salt** of coppered chlorophyllin. Alternatively, the phase-transition-modifying agent within the gel can comprise a...of the present invention can be used for laboratory testing, such as immunoassay systems and **ovulation** testing. Actuators can be constructed using the gels, such as an energy efficient window, wherein...

10/5,K/63 (Item 63 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00131909

ENZYME IMMUNOASSAY WITH TWO-PART SOLUTION OF TETRAMETHYLBENZIDINE AS CHROMOGEN

Patent Applicant/Assignee:

HYGEIA SCIENCES LIMITED PARTNERSHIP,

Inventor(s):

GERBER Bego,
BLOCK Elliott,
BAHAR Izak,
CANTAROW Walter D,
EATON Cheryl,
JONES Wendy E,
COSEO Mary,
BRUINS John B,

Patent and Priority Information (Country, Number, Date):

Patent: WO 8604421 A1 19860731

Application: WO 85US73 19850117 (PCT/WO US8500073)

Priority Application: WO 85US73 19850117

Designated States: DE FR JP

Main International Patent Class: G01N-033/54

International Patent Class: G01N-33:58 ; G01N-33:74 ; G01N-33:76

Publication Language: English

English Abstract

Colorimetric detection of bindable substances such as antibodies and antigens using chromogens of improved sensitivity and stability. The chromogenes take the form of activated solutions containing tetramethylbenzidine or water soluble derivatives of

tetramethylbenzidine. Such chromogens are of particular use in home testing applications for detection of antigens such as human chorionic gonadotropin, human **luteinizing** hormone, and gonococcus bacteria, as well as the detection of antibodies for these substances.

Detailed Description

... oxidoreductases, one might monitor the oxidation of a chromogenic substance by a substrate such as **hydrogen peroxide**. Such so-called **colorimetric** assays are readily adapted to the home -testing environment. When the chromogenic substance oxidizes, it forms a chromophore which exhibits visually discer-nable **color** changes.

Typical enzyme immunoassays include competitive EIA for antigens, and an enzyme linked immunosorbent assay...compounds have been reported as soluble and initially colorless, yielding color change upon oxidation with **hydrogen peroxide**. Typical enzymes that have been used in the enzyme immunoassay methods are horseradish peroxidase, glucose...

...be stable, soluble, and exhibit rapid color change upon reaction. Also, with substrate, e.g., **hydrogen peroxide** when exposed to oxidative enzymes, the product chromophore should likewise be safe, stable, and exhibit...has been used to determine peroxidase activity of hemew proteins. In such an application, benzidine- **hydrogen peroxide** chromogenic substrates have been used in forensic medicine for the detection of blood using the peroxidase activity of hemoglobin. Also, **benzidine** staining procedures have been used to detect the peroxidase actiVity of the heme proteins cytochrome...

...One such alternative reported in the literature is the use of 3,3',5,5'-**tetramethylbenzidine** in **hydrogen peroxide** as a stain for the peroxidase activity of heme proteins, particularly cytochrome P. The results of the improved staining procedures using **betramethylbenzidine** are reported in P. Thomas, B. Ryan, and W. Levin, *Analytical Biochemistry* 75, 168-176 (1976). The advantages of using **tetramethylbenzidine** for the heme staining of cytochrome P-450 as reported in this reference were that the TMB substrates exhibited increased sensitivity, clear dull background, thereby improving **color** contrast, and greater staining stability, i.e., the TMB stained gels could be stored in...

...sample. Quantitative measurement is obtained spectro photometrically by reading the absorbance at maximum absorbance wavelength.

Tetramethylbenzidine and its water soluble chemical derivatives, particularly water soluble inorganic or organic acid **salts** thereof have important advantages over other sensitive chromogens in application to **colorimetric** enzyme immunoassays. An activated chromogen solution of **o - phenylenediamine** (OPD) dissolved in **hydrogen peroxide** shows the characteristic that the OPD chromogen slowly oxidizes to a yellow/orange **color** when left to stand alone without the presence of enzyme. This must be taken into account when actually conducting the assay in the presence of enzyme. By contrast, solutions of **tetramethylbenzidine** in **hydrogen peroxide** or inorganic or organic water soluble **salts** of **tetramethylbenzidine** in **hydrogen peroxide** oxidize to **color** far less rapidly than the OPD **hydrogen peroxide** solution*. Therefore, there is significantly less background **color** development in the case of TMB in **hydrogen peroxide**. Furthermore, solutions of tetramethylbenzidine or its water soluble **salts** have the additional advantage over OPD solutions in that the TMB solutions are very stable when left alone prior to admixture of

11/5/4 (Item 4 from file: 350)
 DIALOG(R)File 350:Derwent WPIX
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007595162

WPI Acc No: 1988-229094/198833

XRAM Acc No: C88-102302

XPX Acc No: N88-174324

Indirect colorimetric detection of analyte - using a ratio of light signals, one of which is at a wavelength where attenuation occurs at increasing concn.

Patent Assignee: BECTON DICKINSON CO (BECT)

Inventor: KRAUTH G H

Number of Countries: 020 Number of Patents: 013

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
EP 278149	A	19880817	EP 87305385	A	19870617	198833 B
JP 63180858	A	19880725	JP 87210024	A	19870824	198835
DK 8702726	A	19880713				198839
AU 8773771	A	19880714				198842
FI 8702432	A	19880713				198842
US 4954435	A	19900904	US 872334	A	19870112	199038
CA 1284947	C	19910618				199129
EP 278149	B1	19920909	EP 87305385	A	19870617	199237
DE 3781672	G	19921015	DE 3781672	A	19870617	199243
			EP 87305385	A	19870617	
FI 88340	B	19930115	FI 872432	A	19870601	199308
ES 2035062	T3	19930416	EP 87305385	A	19870617	199324
JP 94007129	B2	19940126	JP 87210024	A	19870824	199407
DK 169710	B	19950116	DK 872726	A	19870527	199508

Priority Applications (No Type Date): US 872334 A 19870112

Cited Patents: A3...8844; EP 165072; EP 191575; No-SR.Pub; US 4401387; US 4495293; US 4503143

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 278149	A	E	17		
Designated States (Regional): BE CH DE ES FR GB GR IT LI NL SE					
EP 278149	B1	E	18	G01N-033/543	
Designated States (Regional): BE CH DE ES FR GB GR IT LI NL SE					
DE 3781672	G			G01N-033/543	Based on patent EP 278149
FI 88340	B			G01N-033/543	Previous Publ. patent FI 8702432
ES 2035062	T3			G01N-033/543	Based on patent EP 278149
JP 94007129	B2	17		G01N-033/543	Based on patent JP 63180858
DK 169710	B			G01N-033/543	Previous Publ. patent DK 8702726

Abstract (Basic): EP 278149 A

Method for the detection of an analyte in a sample comprises (a) directing an incident light at different wavelengths into a liq. suspension or soln. contg. an analyte of interest, the suspension or soln. being capable of attenuating the amt. of light signal at a first wavelength as a function of the increasing concn. of the analyte present, (b) detecting light signal at the first wavelength and at a second wavelength at which no attenuation of light signal occurs as the concn. of the analyte increases and (c) forming a ratio of the 2 respective wavelengths and comparing the ratio with ratios of known amts. of the analyte to determine the amt. of analyte in the sample. Pref. the light signals detected are light scatter or fluorescence emissions.

USE/ADVANTAGE - Using a ratio of light signals provides a

correction mechanism for obviating such variable as fluctuation in the lamp output, variations in tube position, dia. or optical quality. Use of the ratio also overcomes differences in the concn. of the particulate matter which is added to the admixt. for light detection purposes when light scatter attenuation is used. The method allows for a sensitive detection of the analyte since low concns. of prefd. chromogenic substances affect the deg. of light scatter or fluorescence.

0/6

Title Terms: INDIRECT; COLORIMETRIC; DETECT; ANALYTE; RATIO; LIGHT; SIGNAL; ONE; WAVELENGTH; ATTENUATE; OCCUR; INCREASE; CONCENTRATE

Derwent Class: B04; J04; S03

International Patent Class (Main): G01N-033/543

International Patent Class (Additional): C12Q-001/28; G01J-003/42;

G01N-033/52; G01N-033/54; G01N-033/545; G01N-033/573; G01N-033/76

File Segment: CPI; EPI

11/5/5 (Item 5 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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003652968

WPI Acc No: 1983-12958K/198306

XRAM Acc No: C83-012533

XPX Acc No: N83-024143

Determn. of human chorionic gonadotropin - by enzyme-immunoassay, using solid phase on which monoclonal antibody to HCG is immobilised

Patent Assignee: TOYOCO KK (TOYM)

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
JP 57201853	A	19821210				198306 B

Priority Applications (No Type Date): JP 8187652 A 19810608

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
JP 57201853	A		7		

Abstract (Basic): JP 57201853 A

In the quantitative determination of human chorionic gonadotropin (HCG) by enzyme-immunoassay (EIA), solid phase on which monoclonal antibody to HCG is immobilised is used. Method is used for microdetermination of HCG to detect malignant tumour. By the use of immobilised monoclonal anti-HCG, interference by **luteinizing** hormone (LH) is minimised to improve selectivity of the test method.

In an example, in a plastic test tube, 50 microlitres of the sample (or standard HCG soln.) and 200 microlitres of 0.02 M phosphate buffer soln. (pH 7.5) were mixed. A polystyrene bead on which monoclonal anti-HCG is immobilised was added, and the mixt. shaken. The bead was sepd. from the mixt., and washed with physiological saline soln. The bead was then reacted with commercial polyclonal anti-HCG labelled with peroxidase. In another test tube, the polystyrene bead was reacted with 0.5 mL of substrate soln. contg. 0.3% **o** - **phenylenediamine** and 0.02% **H2O2**. The enzyme reaction was stopped by adding 2 mL of 1N H2SO4, and then absorbence of the mixt. at 492 nm was determined.

Title Terms: DETERMINE; HUMAN; CHORIONIC; GONADOTROPIN; ENZYME; IMMUNOASSAY ; SOLID; PHASE; MONO; CLONE; ANTIBODY; HCG; IMMOBILISE; IMMOBILISE

Derwent Class: A96; B04; D16

International Patent Class (Additional): G01N-033/54
File Segment: CPI

11/5/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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000547853

WPI Acc No: 1967-03834H/196801

Test article for determining the fertile period of women comprises an -
absorbent material impregnated with mannitol-peroxide complex and an o

Patent Assignee: FOSTER RO (WESN)

Number of Countries: 002 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 3406015	A					196801 B
JP 70026673	B					197034

Priority Applications (No Type Date): US 65429619 A 19650201; US 65429619 A
19650201

Abstract (Basic): US 3406015 A

Article for the determination of the fertile period of women
consisting essentially of an absorbent material impregnated with (a) a
mannitol-peroxide complex, and (b) an essentially non-toxic organic
compound, which forms a coloured oxidation product in the presence of
oxygen given off by the peroxide.

The absorbent material may be an absorbent paper, such as
absorbent, chemically-pure filter paper, strips of fabric, or pieces of
porous, absorbent wood. Complex (a) is prepared from mannitol and
aqueous **hydrogen peroxide**. Organic compound (b) is pref. guaiac
resin, but may also be **benzidine**, **o - tolidine**, dianisidine,
phenylenediamine, or 2, 7-diaminofluorene dihydrochloride.

The article is contacted with a saliva specimen from the
test-subject. During the period of fertility and **ovulation** a colour
change occurs in the article, whereas at other periods no colour change
occurs. The test is rapid and easily operated. The test is mainly
intended for human use, but may be also used for animals. The complex
(a) is stable, whereas **hydrogen peroxide** by itself is unstable.

Title Terms: TEST; ARTICLE; DETERMINE; FERTILITY; PERIOD; WOMAN; COMPRISE;
ABSORB; MATERIAL; IMPREGNATE; MANNITOL; PEROXIDE; COMPLEX

Derwent Class: B07; C03

File Segment: CPI

11/5/7 (Item 7 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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000521859

WPI Acc No: 1966-22417F/196800

Test article for determining the fertile period of

Patent Assignee: ULESTON LABS INC (WESN)

Number of Countries: 007 Number of Patents: 007

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
ZA 6600465	A					196800 B
AU 6601069	A					196801
CA 822602	A					196801

FR 1466811	A	196801
NL 6601080	A	196801
JP 70026673	B	197034
DE 1303594	B	197218

Priority Applications (No Type Date): US 65429619 A 19650201

Abstract (Basic): ZA 6600465 A

Article for the determination of the fertile period of women consisting essentially of an absorbent material impregnated with (a) a mannitol-peroxide complex, and (b) an essentially non-toxic organic compound, which forms a coloured oxidation product in the presence of oxygen given off by the peroxide.

The absorbent material may be an absorbent paper, such as absorbent, chemically-pure filter paper, strips of fabric, or pieces of porous, absorbent wood. Complex (a) is prepared from mannitol and aqueous **hydrogen peroxide**. Organic compound (b) is pref. guaiac resin, but may also be **benzidine**, **o - tolidine**, dianisidine, phenylenediamine, or 2,7-diaminofluorene dihydrochloride.

The article is contacted with a saliva specimen from the test-subject. During the period of fertility and **ovulation** a colour change occurs in the article, whereas at other periods no colour change occurs. The test is rapid and easily operated. The test is mainly intended for human use, but may be also used for animals. The complex (a) is stable, whereas **hydrogen peroxide** by itself is unstable.

Title Terms: TEST; ARTICLE; DETERMINE; FERTILITY; PERIOD

Derwent Class: B00

File Segment: CPI

11/TI/1 (Item 1 from file: 350)
DIALOG(R)File 350:(c) 2003 Thomson Derwent. All rts. reserv.

Absorbent article used in sanitary napkins and panty liners has odor control system comprising an oxidizing agent and an absorbent core disposed between liquid permeable top sheet and air permeable back sheet

11/TI/2 (Item 2 from file: 350)
DIALOG(R)File 350:(c) 2003 Thomson Derwent. All rts. reserv.

Absorbent articles e.g. sanitary napkin, pantiliner, tampon, diaper or incontinence pad for controlling odors from body fluids comprise an odor control system containing oxidizing agents and odor absorbing agents

11/TI/3 (Item 3 from file: 350)
DIALOG(R)File 350:(c) 2003 Thomson Derwent. All rts. reserv.

Use of new and known androst-5-en-17beta-yl)alkylsulfoxide or sulfone compounds for controlling fertility

Set	Items	Description
S1	2941	OVULAT? OR MENSTRUAT? OR LUTEINIZ? OR LUTEINIS?
S2	36132	HYDROGEN() PEROXIDE OR H2O2
S3	323514	COLOR???
S4	506465	BENZIDINE OR TETRAMETHYLBENZIDINE OR DIAMINOBENZIDINE OR S- ALT? ? OR 3()AMINO()9()ETHYLCARBAZOLE OR 4()METHOXY(2W)NAPHTH- OL OR O() (TOLIDINE OR DIANISIDINE OR METHOXYPHENOL OR PHENYLE- NEDIAMINE) OR 5()AMINOSALICYLIC OR PYROGALLOL
S5	7	S1 AND S2 AND (S3 OR S4)
S6	7	IDPAT (sorted in duplicate/non-duplicate order)
S7	7	IDPAT (primary/non-duplicate records only)
S8	592421	S3 OR COLOUR???
S9	7	S1 AND S2 AND (S3 OR S4)
S10	7	IDPAT (sorted in duplicate/non-duplicate order)
S11	7	IDPAT (primary/non-duplicate records only)

? show files

File 347:JAPIO Oct 1976-2002/Nov(Updated 030306)

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File 350:Derwent WPIX 1963-2003/UD,UM &UP=200317

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File 371:French Patents 1961-2002/BOPI 200209

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hydrogen peroxide , whereas OPD has the tendency to oxidize slowly even when in water solution...

10/5,K/64 (Item 64 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00103983

SPECIFIC IMPENDING OVULATION INDICATOR
INDICATEUR SPECIFIQUE D' OVULATION IMMINENTE

Patent Applicant/Assignee:

OSTER G,
KESTON A,

Inventor(s):

OSTER G,
KESTON A,

Patent and Priority Information (Country, Number, Date):

Patent: WO 8002800 A1 19801224

Application: WO 80US813 19800620 (PCT/WO US8000813)

Priority Application: US 7950810 19790621

Designated States: JP AT CH DE FR GB LU NL SE

Main International Patent Class: A61K-039/00

International Patent Class: C12Q-01:28; C12Q-01:66; G01N-33:48

Publication Language: English

English Abstract

Method for detecting impending **ovulation** in the human female by testing means employable by the average person. The test method involves contacting vaginal fluid samples with a bibulous mat containing an antibody against estrogen-induced peroxidase. The mat is then washed and tested for peroxidase.

Detailed Description

This invention relates to methods of detecting impending **ovulation** in human females, including methods which are sufficiently simple so that a woman can carry...

...of peroxidase with a hydroperoxide and-a chromogenic substrate of peroxidase.

The hydroperoxide may be **hydrogen peroxide** or a hydroperoxide generating system, such as the inorganic peroxides, sodium peroxide, barium peroxide, strontium...

...green (to produce malachite green) and leucophenol phthalein (desirably employed in an alkaline medium);

6) **Colored** dyes, such as 2,6 dichlorophenol indo phenol;

7) Various biological substances, such as epinephrine, the flavones, tyrosine, dihydrophenyl alanine (producing an orange-reddish **color**) and tryptophane, Other substances such as gum guaiac, guaiaconic acid, Nadi reagent (producing a bluish **color**), bilirubin (producing a greenish **color**), iodides (which produce a brown **color** and, if starch is present, produce a deep blue **color** which is much stronger than iodide alone) .

Some of the substances may be most effectively...

Claim

... pressed against starch iodide test paper and the test paper is moistened with 0.01% **hydrogen peroxide** . A strong blue **color** is regarded as a positive test and weak or no **coloration** is regarded as a negative test, For best results it is preferable to start on...

...6 for the daily routine. The first positive test may be taken to indicate that **ovulation** is impending and y will follow within two or three days. In place of starch-iodide test paper, filter paper impregnated with 3.3',5,5' **tetramethylbenzidine** and potassium thiocyanate, impregnated with p,pl biphenol and sodium thiocyanate, or guaiac, or orthotolidine...

10/5,K/65 (Item 65 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00103779

IMPENDING OVULATION TEST

PROCEDE DE DETERMINATION D'UNE OVULATION IMMINENTE

Patent Applicant/Assignee:

OSTER G,
KESTON A,

Inventor(s):

OSTER G,
KESTON A,

Patent and Priority Information (Country, Number, Date):

Patent: WO 8002596 A1 19801127

Application: WO 80US618 19800516 (PCT/WO US8000618)

Priority Application: US 7939273 19790516

Designated States: JP AT CH DE FR GB LU NL SE

Publication Language: English

English Abstract

Method for detecting impending **ovulation** in the human female by testing means employable by the average person. The test method involves contacting vaginal fluid samples with chemicals that indicate the presence of peroxidase in the vaginal fluid samples, e.g. a chromogenic substrate of peroxidase mixed with a hydroperoxide.

Detailed Description

This invention relates to methods of detecting impending ovulation in human...

...forms of the test involves the use of a paper comprising starch and an iodide **salt** which produces a blue **color** in the presence of a peroxidase when moistened with **hydrogen peroxide** . When peroxidase is present in the vaginal fluid the aforesaid test sheet will turn blue...

...gave a strong color (i.e. a positive test).

Here again the test presumably anticipated **ovulation** .

In place of ortho-tolidine a number of chromogenic substrates may be used, such as...

10/TI/1 (Item 1 from file: 348)

DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Polypeptide and process for measuring living body components using the same
Polypeptide und Verfahren zur Messung von Komponenten eines Lebniskorpers
durch deren Gebrauch

Polypeptides et procede de mesure de composants dans un organisme vivant
les moyennant

10/TI/2 (Item 2 from file: 348)

DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Particles having an incorporated composition comprising a chemiluminescent
compound

Teilchen enthaltende eine Zusammensetzung die eine chemilumineszierende
Verbindung enthalt

Particules contenant une composition comprenant un compose
chimiluminescent

10/TI/3 (Item 3 from file: 348)

DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

A homogeneous assay for determining analyte

Homogenes Testsystem zur Bestimmung eines Analytes

Essai homogene pour determiner un analyte

10/TI/4 (Item 4 from file: 348)

DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Vascular smooth muscle cell growth factor

Wachstumsfaktor fur Zellen der glatten Gefassmuskulatur

Facteur de croissance pour des cellules des muscles vasculaires lisses

10/TI/5 (Item 5 from file: 348)

DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

USE OF VANADIUM BROMOPEROXIDASE AS A SIGNAL-GENERATING ENZYME FOR
CHEMILUMINESCENT SYSTEMS: TEST KITS AND ANALYTICAL METHODS

VERWENDUNG EINER VANADIN-BROMPEROXIDASE ALS EIN SIGNALGENERIERENDES ENZYM
FUR CHEMILUMINESZIERENDE SYSTEME: TESTKITS UND ANALYTISCHE VERFAHREN

KITS D'ESSAI ET PROCEDES D'ANALYSE DANS LESQUELS LA BROMOPEROXYDASE DE
VANADIUM EST UTILISEE COMME ENZYME GENERATRICE DE SIGNAUX POUR DES
SYSTEMES A CHIMIOLUMINESCENCE

10/TI/6 (Item 6 from file: 348)

DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Polypeptide and process for measuring living body components using the same
Polypeptide und Verfahren zur Messung von Komponenten eines Lebniskorpers
durch deren Gebrauch

Polypeptides et procede de mesure de composants dans un organisme vivant
les moyennant

10/TI/7 (Item 7 from file: 348)
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Method and device for specific binding assay
Methode und Vorrichtung fur eine Bestimmung durch spezifische Bindung
Methode et dispositif a utiliser dans les essais de liaisons specifiques

10/TI/8 (Item 8 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Electrochemical assay method and novel p-phenylenediamine compound
Elektrochemische Bestimmungsmethode und neue p-Phenylendiamin-Verbindung
Methode d'essai electrochimique et compose de p-phenylenediamine nouveau

10/TI/9 (Item 9 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Assay methods utilizing induced luminescence
Bestimmungsmethoden unter Verwendung von induzierter Lumineszenz
Methodes d'essai employant luminescence induite

10/TI/10 (Item 10 from file: 348)
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Process and device for specific binding assay
Verfahren und Vorrichtung zur Verwendung in spezifischen Bindungstests
Procede et dispositif a utiliser dans les essais de liaisons specifiques

10/TI/11 (Item 11 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Process and device for specific binding assay.
Verfahren und Vorrichtung fur spezifische Bindungsassay.
Procede et dispositif d'essai de liaisons specifiques.

10/TI/13 (Item 13 from file: 348)
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HUMAN INTRA-ACROSOMAL SPERM ANTIGEN FOR USE IN A CONTRACEPTIVE VACCINE
MENSCHLICHES INTRA-AKROSOMALES SPERMAANTIGEN ZUR VERWENDUNG IN EINEM
EMPFANGNISVERHUTUNGSIMPFSTOFF
ANTIGENE INTRA-ACROSOMAL DU SPERME HUMAIN ET SON UTILISATION DANS UN VACCIN
CONTRACEPTIF

10/TI/14 (Item 14 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Reaction vessel.
Reaktionsgefass.
Recipient pour reactions.

10/TI/15 (Item 15 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Anti-hCG-beta core monoclonal antibody, its production and use.
Monoklonaler Antikörper gegen Kern-hCG-beta, seine Herstellung und
Verwendung.
Anticorps monoclonal contre le hCG-beta a noyau, sa production et son
utilisation.

10/TI/16 (Item 16 from file: 348)
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Agent for determining manganese and method relating thereto.
Agent zur Bestimmung von Mangan und Verfahren in Verbindung damit.
Agent pour determiner du manganese et methode afferent a cela.

10/TI/18 (Item 18 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Analytic reader device.
Gerat zum Ablesen analytischer Tests.
Dispositif de lecture analytique.

10/TI/19 (Item 19 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Improved dipstick device for assays.
Teststab.
Batonnet pour essais.

10/TI/20 (Item 20 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Antibody to polypeptides complementary to peptides or proteins having an
amino acid sequence or nucleotide coding sequence at least partially
known and methods
Antikörper gegen Polypeptide, die gegen Peptide oder Proteine mit
mindestens teilweise bekannter Aminosäure oder kodierender
Nukleotidsequenz komplementär sind
Anticorps contre des polypeptides complementaires de peptides ou proteines
ayant une sequence d'acides amines ou une sequence de nucleotides
codants au moins pa

10/TI/22 (Item 22 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

A new universally applicable detection system based on ultra small
colloidal metal particles.
Auf ultrakleine kolloidale Metallteilchen gegründetes, allgemein
anwendbares Nachweissystem.
Systeme de detection universellement applicable base sur des particules
colloïdales de metal ultra-petites.

10/TI/24 (Item 24 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Assays.
Assays.
Essais.

10/TI/25 (Item 25 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Indirect colorimetric detection of an analyte in a sample using ratio of light signals.
Indirekte kolorimetrische Detektion eines Analyten in einer Probe unter Zuhilfenahme des Verhältnisses von Lichtsignalen.
Detection colorimetrique indirecte d'un analyte dans un echantillon en ayant recours au rapport entre des signaux de lumiere.

10/TI/26 (Item 26 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Solid phase immunoassay method.
Festphasen-Immuntestverfahren.
Procede de dosage immunologique en phase solide.

10/TI/27 (Item 27 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Detection of haptens in immunoassay techniques.
Nachweis von Haptenen in Immunotestverfahren.
Detection d'haptenes dans des techniques d'immunoessai.

10/TI/28 (Item 28 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

METHOD OF IMMUNOASSAY.
IMMUNTESTVERFAHREN.
PROCEDE D'IMMUNOANALYSE.

10/TI/30 (Item 30 from file: 348)
DIALOG(R)File 348:(c) 2003 European Patent Office. All rts. reserv.

Multizone analytical element for immunoassays having detectable signal concentrating zone.
Mehrschichtiges analytisches Element fur Immunoassays mit einer Schicht zum Konzentrieren des Nachweisbarsignals.
Element analytique multicouche pour des essais immunologiques ayant une couche pour concentrer le signal detectable.

10/TI/31 (Item 31 from file: 349)
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INDIVIDUALIZATION OF THERAPY WITH ANTINEOPLASTIC AGENTS
PERSONNALISATION D'UNE THERAPIE A L'AIDE D'AGENTS ANTINEOPLASQUES

10/TI/32 (Item 32 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

FLOW THROUGH ASSAY DEVICE, DIAGNOSTIC KIT COMPRISING SAID ASSAY DEVICE AND
USE OF SAID ASSAY DEVICE IN THE DETECTION OF AN ANALYTE PRESENT IN A
SAMPLE
DISPOSITIF D'ESSAI EN CONTINU, TROUSSE DE DIAGNOSTIC COMPRENANT LEDIT
DISPOSITIF ET UTILISATION DE CE DISPOSITIF POUR LA DETECTION D'UN
ANALYTE DANS UN ECHANTILLON

10/TI/34 (Item 34 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

METHODS AND COMPOSITIONS FOR IN VITRO TARGETING
PROCEDES ET COMPOSITIONS UTILISES POUR LE CIBLAGE IN VITRO

10/TI/35 (Item 35 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

LEUCINE-RICH REPEAT-CONTAINING G-PROTEIN COUPLED RECEPTOR-8 MOLECULES AND
USES THEREOF
MOLECULES DU RECEPTEUR 8 COUPLE A LA PROTEINIE G CONTENANT DES REPETITIONS
RICHES EN LEUCINES, ET UTILISATIONS ASSOCIEES

10/TI/37 (Item 37 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

PRODUCTION AND USE OF PROTEIN VARIANTS HAVING MODIFIED IMMUNOGENECITY
VARIANTS DE PROTEINES A IMMUNOGENICITE MODIFIEE

10/TI/38 (Item 38 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

COMPOSITIONS FOR DETECTION OF MULTIPLE ANALYTES
COMPOSITIONS SERVANT A LA DETECTION D'ANALYTES MULTIPLES

10/TI/39 (Item 39 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

DIAGNOSTIC ASSAY FOR ENDOMETRIOSIS
DOSAGE DIAGNOSTIQUE DE L'ENDOMETRIOSE

10/TI/40 (Item 40 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

DIAGNOSTIC ASSAY FOR ENDOMETRIOSIS
ESSAI DIAGNOSTIQUE POUR ENDOMETRIOSE

10/TI/41 (Item 41 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

BETA-LIKE GLYCOPROTEIN HORMONE POLYPEPTIDE AND HETERODIMER
HETERODIMERE ET POLYPEPTIDE D'HORMONE DE GLYCOPROTEINE DE TYPE BETA

10/TI/42 (Item 42 from file: 349)
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PLASMINOGEN ACTIVATOR ASSAY INVOLVING AN ELASTASE INHIBITOR
PARTICULES UTILISEES A DES FINS DIAGNOSTIQUES ET THERAPEUTIQUES

10/TI/45 (Item 45 from file: 349)
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PRENATAL DIAGNOSTIC METHODS
PROCEDES DE DIAGNOSTIC PRENATAL

10/TI/46 (Item 46 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

TREATMENT AND DIAGNOSIS OF INFERTILITY USING TGF'beta' OR ACTIVIN
TRAITEMENT ET DIAGNOSTIC D'UNE STERILITE PAR LE TGF-'beta' OU L'ACTIVINE

10/TI/48 (Item 48 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

POSITIVELY CHARGED NON-NATURAL AMINO ACIDS, METHODS OF MAKING THEREOF, AND
USE THEREOF IN PEPTIDES
ACIDES AMINES NON NATURELS ET CHARGES POSITIVEMENT, PROCEDES DE SYNTHESE
CORRESPONDANTS ET UTILISATION DE CES ACIDES AMINES DANS DES PEPTIDES

10/TI/49 (Item 49 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

HUMAN TYPE II GONADOTROPIN-RELEASING HORMONE RECEPTOR
RECEPTEUR HUMAIN DE L'HORMONE DE LIBERATION DE LA GONADOTROPHINE DE TYPE II

10/TI/50 (Item 50 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

CHEMILUMINESCENT COMPOSITIONS AND THEIR USE IN THE DETECTION OF HYDROGEN
PEROXIDE
COMPOSITIONS CHIMIOLUMINESCENTES ET LEUR UTILISATION DANS LA DETECTION DE
PEROXYDE D'HYDROGENE

10/TI/51 (Item 51 from file: 349)
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DETERMINATION AND MONITORING OF BLADDER CANCER
DETERMINATION ET CONROLE DE L'EVOLUTION DU CANCER DE LA VESSIE

10/TI/52 (Item 52 from file: 349)
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COLOR HEAT MOUNT DETECTORS
DETECTEURS CHROMATIQUES DE MONTE EN PERIODE DE CHALEURS

10/TI/53 (Item 53 from file: 349)
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TRANSPARENT ASSAY TEST DEVICES AND METHODS
DISPOSITIFS TRANSPARENTS POUR ANALYSES, ET PROCEDES ASSOCIES

10/TI/54 (Item 54 from file: 349)
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NOVEL CHEMILUMINESCENT COMPOUNDS AND METHODS OF USE
NOUVEAUX COMPOSES CHIMILUMINESCENTS ET PROCEDES D'UTILISATION

10/TI/56 (Item 56 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

AN ASSAY METHOD USING INTERNAL CALIBRATION TO MEASURE THE AMOUNT OF ANALYTE
IN A SAMPLE
PROCEDE D'ANALYSE UTILISANT L'ETALONNAGE INTERNE POUR MESURER LA QUANTITE
D'ANALYTE DANS UN ECHANTILLON

10/TI/57 (Item 57 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

ANTIBODY TO PITUITARY ADENYLATE CYCLASE ACTIVATING PEPTIDE-PACAP, HYBRIDOMA
AND ASSAY FOR PACAP
ANTICORPS DE PEPTIDE ACTIVATEUR DE CYCLASE D'ADENYLATE PITUITAIRE (PACAP),
HYBRIDOME ET ANALYSE DE PACAP

10/TI/58 (Item 58 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

POLYPEPTIDE ANALOGS OF APOLIPOPROTEIN E, DIAGNOSTIC SYSTEMS AND METHODS
USING THE ANALOGS
ANALOGUES POLYPEPTIDES D'APOLIPOPROTEINE E, SYSTEMES DIAGNOSTIQUES ET
PROCEDES UTILISANT LES ANALOGUES

10/TI/59 (Item 59 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

NOVEL CHEMILUMINESCENT FUSED POLYCYCLIC RING-CONTAINING 1,2-DIOXETANES AND
ASSAYS IN WHICH THEY ARE USED
NOUVEAUX 1,2-DIOXETANES CHIMILUMINESCENTS CONTENANT UN ANNEAU POLYCYCLIQUE
FUSIONNE, ET ANALYSES LES UTILISANT

10/TI/60 (Item 60 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

ASSAYS
ANALYSES

10/TI/61 (Item 61 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

SOLID PHASE IMMUNOASSAY METHOD
PROCEDE IMMUNOANALYTIQUE EN PHASE SOLIDE

10/TI/62 (Item 62 from file: 349)
DIALOG(R)File 349:(c) 2003 WIPO/Univentio. All rts. reserv.

POLYPEPTIDES COMPLEMENTARY TO PEPTIDES OR PROTEINS HAVING AN AMINO ACID
SEQUENCE OR NUCLEOTIDE CODING SEQUENCE AT LEAST PARTIALLY KNOWN AND
METHODS OF DESIGN THEREFOR



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(54) Title: IMPENDING OVULATION TEST (57) Abstract <p>Method for detecting impending ovulation in the human female by testing means employable by the average person. The test method involves contacting vaginal fluid samples with chemicals that indicate the presence of peroxidase in the vaginal fluid samples, e.g. a chromogenic substrate of peroxidase mixed with a hydroperoxide.</p>		

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DescriptionImpending Ovulation TestTechnical Field

This invention relates to methods of detecting
5 impending ovulation in human females, including methods
which are sufficiently simple so that a woman can carry
out the test on herself without the aid of a physician.

Background Art

While prior methods of fertility or ovulation testing
10 have been proposed, prior tests have one or more undesirable aspects. For example, in the prior art the method of utilizing thermometry (the basal body temperature method) provides information on fertility, but this
test merely indicates that ovulation has already occurred
15 and does not detect impending ovulation.

The prior ovulation detection methods involving an examination of cervical mucus for its flow properties, saline content, glucose content and the like, are also deficient in that they do not easily lend themselves
20 to self-examination by the woman and require sampling of portions of the vagina. Similarly, microscopic examination of vaginal cells for staining characteristics and morphology require expensive apparatus and involve techniques which are usually beyond the skill of the
25 average woman. Estrogen analysis of blood and urine is likewise complicated and difficult to carry out.

Means for peroxidase testing have been known since 1898. Such means have been used for over 75 years for the detection of blood, including commercial articles
30 sold, for example, by Smith Kline and French Laboratories and by Miles Laboratories, for the detection of occult blood in urine and feces. Despite the long history



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of the peroxidase test it has not been previously used to determine the surge in estrogen-induced peroxidase in vaginal fluid for the detection of impending ovulation. This may be due to the fact that pathological conditions or injuries resulting in blood being present in the vagina contribute to a false positive indication for estrogen-induced peroxidase. It is known that hemoglobin and its degradation products exhibit a peroxidase-like reaction and, indeed, this property is utilized in the occult blood test for urine and feces.

Disclosure of Invention

In the approximately two to three days prior to ovulation in the menstrual cycle of normal human females there is a surge in the amount of estrogen-induced peroxidase in the vaginal fluid. A simple form of the invention contemplates the woman taking a sample of vaginal fluid with, for example, a moistened cotton swab and contacting the swab with a bibulous material comprising a substance which will cause a visible change in the presence of peroxidase and a peroxide. Such visible change could be a change in color or in luminescence. The finding that the peroxidase is present in the vaginal fluid makes it possible for a woman to readily obtain a sample with a moistened cotton swab with no harm to herself.

One of the preferred forms of the test involves the use of a paper comprising starch and an iodide salt which produces a blue color in the presence of a peroxidase when moistened with hydrogen peroxide. When peroxidase is present in the vaginal fluid the aforesaid test sheet will turn blue.

Some of the means used in this invention detect both peroxidase and peroxidase-like substances, such as hemoglobin and its degradation products.



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Best Mode For Carrying Out the Invention

A simple method for the detection of impending ovulation in women, as in the present invention, is of the highest importance to the human race and is of paramount interest to such prestigious organizations as the Population Council, the Ford Foundation, the National Institutes of Health and the World Health Organization. With the present invention a woman can, by herself, determine her impending fertile time. There is extensive clinical evidence that for women the fertile time commences within 12 to 72 hours of ovulation (C. Tietze Fertility and Sterility, Vol. 11, p. 485, 1960). By abstaining from coitus or by otherwise protecting herself from insemination during the fertile time a woman can avoid pregnancy. Thus with the aid of the present invention which enables a woman to determine her fertile time, this form of birth control could, if practiced widely, substantially reduce the rate of world-population growth. Using the present invention one may practice birth control without interference with the normal female hormonal function, such as occurs with the contraceptive pill which is objectionable to certain segments of the world population on religious grounds, as well as to others on medical grounds due to the possible serious side effects. A woman practicing abstinence during the fertile period as determined by the present invention may avoid the need for contraceptive devices, such as the intrauterine device, for birth control which are considered undesirable to some.

The present invention may also be an aid to couples who wish to have a child, but have failed because, for example, incorrect timing of coitus. Thus it may be seen that because the present invention can be a valuable aid in family planning, it serves an important humanitarian purpose.



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A preferred embodiment of the present invention uses a chromogenic substrate which responds rapidly to the estrogen-induced peroxidase of the vagina in the presence of a peroxide, but responds much more slowly to the action of hemoglobin or its degradation products. Such chromogenic substrates are characterized by the fact that the rate constant (commonly designated k_4 ; see B. Chance, Advances in Enzymology, 1951, Volume 12, pages 153-180) for the reaction of the substrate with the peroxidase-peroxidide complex exceeds about 10^5 moles⁻¹ seconds⁻¹. Substrates having such high values of k_4 include, for example, p,p¹ biphenol, hydroquinone and 0-phenylenediamine. It should be noted that values of k_4 for a given chromogenic substance may differ somewhat with the choice of the particular hydroperoxide employed.

One of the preferred embodiments involves impregnating a bibulous strip of paper with an inorganic peroxide such as hydrogen peroxide, sodium peroxide, barium peroxide, strontium peroxide, sodium perborate, and the like or an organic peroxide, such as methyl hydroperoxide, ethyl hydroperoxide, cumene hydroperoxide, dimethoxy dihydroperoxy hexane, and the like. Hydrogen peroxide may be considered both an inorganic peroxide and as a hydroperoxide. Many compounds, for example sodium peroxide, barium peroxide, strontium peroxide, sodium perborate, and the bis (1-hydroxyalkyl) peroxides generate hydrogen peroxide when moistened. Enzymatic reactions such as the action in air of L-amino oxidase on L-amino acids also generate hydrogen peroxide.

Chromogenic peroxidase substrates which may be employed in the present invention include the following substances:

- 1) Monoamines, such as aniline and its derivatives, orthotoluidine, para-toluidine, etc.;



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- 2) Diamines, such as ortho-phenylenediamine, N,N dimethylpara-phenylenediamine, N,N diethyl-phenylenediamine, benzidine, 3,3', 5,5', tetramethyl benzidine, dianisidine, o-tolidine, etc.;
- 5 3) Phenols, such as phenol per se, thymol, ortho, meta and para-cresols, alpha-naphthol, p,p-dihydroxybiphenyl, phloroglucinol and guaiacol;
- 4) Aromatic acids, such as salicylic, pyrocatechuic and gallic acids;
- 10 5) Leucodyes, such as leucomalachite green (to produce malachite green) and leucophenolphthalein (desirably employed in an alkaline medium);
- 6) Colored dyes, such as 2,6 dichlorophenol indophenol;
- 15 7) Various biological substances, such as epinephrine, the flavones, tyrosine, dihydrophenylalanine (producing an orange-reddish color) and tryptophane. Other substances such as gum guaiac, guaiaconic acid, Nadi reagent (producing a
- 20 bluish color), bilirubin (producing a greenish color), iodides (which produce a brown color and, if starch is present, produce a deep blue color which is much stronger than iodide alone).

25 Some of the substances may be most effectively used in combination rather than individually. For example, Nadi reagent is such a mixture, namely naphthol and p-phenylenediamine, which gives a better final color than the individual components. Another example is

30 a mixture of 4-amino antipyrine and 1,7 dihydroxynaphthalene.

Many of the chromogens, notably benzidine and its derivatives give a more intense color if halogen ions, such as iodide and bromide ions, or if halogenoid ions, such as thiocyanate and selenocynate ions, are present.

35 One of the preferred embodiments of the invention comprises 3,3', 5,5' tetramethyl benzidine and potassium



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thiocyanate; this mixture yields an intense blue color in a positive test.

Substrates which change their fluorescence in the presence of a peroxidase and hydrogen peroxide include
5 a loss of fluorescence of scopoletin or a production of fluorescence with, for example, dichlorofluorescein or homovanillic acid. Chemiluminescence is produced in the presence of peroxidases and hydrogen peroxide for the following typical substances, luminol, zinc
10 tetra phenylporphyrine and the like.

The color forming substance may undergo color change, not as a result of the direct action of a hydroperoxide, but by mediation through another compound which is acted upon by a hydroperoxide and does not itself become highly
15 colored. Examples of such color-forming or color-changing substances are:

- 1) Starch and potassium iodide to produce the characteristic starch-iodine purple which is stronger in color than iodide alone produces.
- 20 2) Mixture of a ferrous salt, such as ferrous ammonium sulfate, and tannic acid to produce a dark color.
- 3) Mixture of potassium iodide and 3,3', 5,5' ~~tetramethyl benzidine~~ to produce a blue-black
25 color stronger than either one alone.
- 4) Mixture of potassium thiocyanate and o-tolidine forming a blue color stronger than o-tolidine alone.
- 5) Mixture of potassium thiocyanate and p, p' biphenol forming a black color stronger than
30 p,p' biphenol alone.

Hereinafter such mixtures will also be referred to as chromogenic substrates of peroxidase, even if the mixture does not undergo a color change as a result
35 of the direct action of a hydroperoxide.



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Example 1

A woman who has regular menstrual cycles donated vaginal samples daily starting on day 5 of her cycle, where day 1 is taken as the day when menstruation began.

5 The vaginal samples were obtained by the woman using a standard six inch cotton-tipped swab ("Puritan", Hardwood Products Co.). The cotton end was moistened with water and rolled gently on the wall of the anterior vagina. The vaginal sample on the swab was divided into six

10 parts, each part of which was kept moistened.

One portion of the daily sample was contacted with commercially-available starch-iodide test paper (Precision Laboratories) and on the paper was placed a drop of dilute aqueous hydrogen peroxide solution having a concentration of 0.005%. A positive test was indicated by

15 the formation of a strong blue color in about 2 minutes. A negative test was indicated if no color or only weak color was produced in about 2 minutes.

For the woman tested the test was negative for

20 the samples of days 5 through 8, but on days 9 and 10 a strong blue color (i.e. positive color) was obtained. On this same woman tests of lutenizing hormone (LH) were taken on daily samples of her urine and it was found that a surge in LH occurred on day 12. She reported

25 that her cervical mucus felt slippery (the Billing Test) at days 11 and 12 and that her basal body temperature (BBT) rose on day 14. The woman started to menstruate on day 27. The test for peroxidase herein described occurred at a time consistent with the other tests and

30 therefore the positive peroxidase result anticipated ovulation; ovulation presumably occurring on or about day 13.



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Example 2

A portion of daily vaginal sample as described in example 1 was dipped into a 0.01% aqueous solution of orthotolidine (made up by diluting a 1% ethanolic solution of ortho-

5 tolidine with 0.01 molar phosphate buffer at pH 6.5) and then dipped into a 0.005% solution of hydrogen peroxide. Vaginal samples of days 5 through 8 gave no color (i.e. a negative test) but samples of days 9 and 10 gave a strong color (i.e. a positive test).

10 Here again the test presumably anticipated ovulation.

In place of ortho-tolidine a number of chromogenic substrates may be used, such as guaiac, p,p' biphenol or 3,3' 5,5' tetramethylbenzidine. Said o-tolidine, p,p' biphenol or tetramethylbenzidine solutions may

15 also comprise a bromide, iodide or thiocyanate. Instead of solutions of the above chromogenic substrates, a bibulous mat, for example paper, comprising them may be employed. After contact with the swab comprising the vaginal sample the bibulous mat is moistened with

20 hydrogen peroxide to produce the color indication if peroxidase is present.

One may also use dichlorofluorescein in place of ortho-tolidine but now a positive test is a strong yellow fluorescence (as observed under Wood's Lamp illumination)

25 while no or only weak fluorescence is a negative test.

Example 3

A portion of the daily vaginal sample as described in example 1 was subjected to the commercially-available "Hematest" test for occult blood (Ames Company). The

30 vaginal sample is applied to the bibulous white paper provided, to which a moistened pill containing, according to the manufacturer, ortho-tolidine, strontium peroxide, calcium acetate and tartaric acid is contacted. Vaginal samples of days 5 through 8 gave no color or only weak



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color, but samples of days 9 and 10 gave a strong blue color. Here again the test presumably anticipated ovulation.

Example 4

5 A portion of the daily vaginal sample as described
in example 1 was subjected to the occult blood test
portion of the commercially-available "N-Multistix"
(Ames Company). According to the manufacturer this
portion of the test stick contains ortho-tolidine and
10 cumene hydroperoxide. The test stick gave no or only
weak coloration for vaginal samples of days 5 through
8, but gave a strong blue coloration for samples of
days 9 and 10. Here again the test presumably anticipated
ovulation.

Example 5

15 A portion of the daily vaginal samples as described
in example 1 was subjected to the commercially-available
"Hemoccult" occult blood test for feces (Smith Kline
and French Laboratories). According to the manufacturer
20 this consists of a bibulous paper impregnated with an
ethanolic solution of guaiac and allowed to dry. The
vaginal samples were contacted with this test paper
and then a 0.1% ethanolic solution of hydrogen peroxide
was added. The test paper gave no or only weak coloration
25 for vaginal samples of days 5 through 8, but gave a
strong blue coloration for samples of days 9 and 10.
Here again the test presumably anticipated ovulation.



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Claims

1. A method for detecting impending ovulation in human females comprising a test for peroxidase in a vaginal fluid sample.
- 5 2. A method according to claim 1 in which said test for peroxidase produces a color change.
3. A method according to claim 1 in which said test for peroxidase produces a change in luminescence.
- 10 4. A method according to claim 1 where the test for peroxidase comprises treating a vaginal fluid sample with a chromogenic substrate of peroxidase and a hydroperoxide.
- 15 5. A method according to claim 4 where the test for peroxidase comprises contacting vaginal fluid with an inorganic peroxide.
6. A method according to claim 1 where the test for peroxidase comprises contacting the vaginal fluid sample with a bibulous mat comprising a chromogenic substrate of peroxidase.
- 20 7. A claim according to claim 1 where the test for peroxidase comprises contacting the vaginal fluid sample with a bibulous mat, said mat comprising a chromogenic substrate for peroxidase and a hydroperoxide.
- 25 8. A claim according to claim 5 where the test for peroxidase comprises contacting a vaginal fluid sample with a chromogenic substrate for peroxidase and an inorganic peroxide in a pill.



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9. A claim according to claim 6 where the chromogenic substrate of peroxidase is guaiac.
10. A claim according to claim 7 where the chromogenic substrate for peroxidase is 0-tolidine and the hydroperoxide is cumene hydroperoxide
11. A claim according to claim 8 where the chromogenic substrate for peroxidase is 0-tolidine and the inorganic peroxide is strontium peroxide.
12. A claim according to claim 4 where the vaginal fluid sample is absorbed on a bibulous material which has been in contact with the vagina.
13. A claim according to claim 4 where the chromogenic substrate is starch and a soluble iodide salt.
14. A claim according to claim 4 where the chromogenic substrate is guaiac.
15. A claim according to claim 4 where the chromogenic substrate has a rate constant k_4 (as defined herein) in excess of about 100,000.
16. A claim according to claim 4 where the chromogenic substrate is p,p' biphenol
17. A claim according to claim 4 where the chromogenic substrate is ortho-tolidine and a soluble iodide salt.
18. A claim according to claim 4 where the chromogenic substrate is 3,3',5,5' tetramethylbenzidine and a soluble iodide salt.



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19. A claim according to claim 4 where the chromogenic substrate is 3,3',5,5' tetramethylbenzidine and a soluble bromide salt.
- 5 20. A claim according to claim 4 where the chromogenic substrate is 3,3',5,5' tetramethylbenzidine and a soluble thiocyanate salt.
21. A claim according to claim 4 where the chromogenic substrate is orthodianisidine and a soluble iodide salt.
- 10 22. A claim according to claim 4 where the chromogenic substrate changes its luminescence after oxidation by peroxide in the presence of peroxidase.
23. A claim according to claim 4 where the hydroperoxide is hydrogen peroxide.
- 15 24. A claim according to claim 4 where the hydroperoxide is cumene hydroperoxide.
25. A claim according to claim 4 where the chromogenic substrate is a mixture of p,p' biphenol and a soluble thiocyanate salt.
- 20 26. A method according to claim 12 where the bibulous mat which has been in contact with the vagina comprises a chromogenic substrate for peroxidase.
27. A claim according to claim 26 where the chromogenic substrate for peroxidase is guaiac.
- 25 28. A claim according to claim 26 where the chromogenic substrate for peroxidase is bilirubin.



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29. A claim according to claim 7 where the chromogenic substrate is o-tolidine and the hydroperoxide is dimethoxy dihydroperoxy hexane.
- 5 30. A claim according to claim 1 where the test for peroxidase comprises contacting a vaginal fluid sample with a compound which generates hydrogen peroxide.
- 10 31. A claim according to claim 1 where the test for peroxidase comprises contacting a vaginal fluid sample with an enzyme-substrate system which generates hydrogen peroxide.



INTERNATIONAL SEARCH REPORT

International Application No

PCT/US80/00618

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ³ According to International Patent Classification (IPC) or to both National Classification and IPC INT. CL. ⁹ G01N 33/00; C12Q 1/28 U.S. CL. 435/28,806; 23/230B,917														
II. FIELDS SEARCHED <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black; margin: 5px 0;">Minimum Documentation Searched ⁴</div> <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 25%; border-bottom: 1px solid black;">Classification System</th> <th style="border-bottom: 1px solid black;">Classification Symbols</th> </tr> <tr> <td style="border: 1px solid black; padding: 5px;">U.S.</td> <td style="border: 1px solid black; padding: 5px;">435/28,806; 23/230B,917</td> </tr> </table> <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black; margin: 5px 0;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁵</div>			Classification System	Classification Symbols	U.S.	435/28,806; 23/230B,917								
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III. DOCUMENTS CONSIDERED TO BE RELEVANT ¹⁴ <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 10%; border-bottom: 1px solid black;">Category [*]</th> <th style="border-bottom: 1px solid black;">Citation of Document, ¹⁶ with indication, where appropriate, of the relevant passages ¹⁷</th> <th style="width: 15%; border-bottom: 1px solid black;">Relevant to Claim No. ¹⁸</th> </tr> <tr> <td style="border: 1px solid black; text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="border: 1px solid black; padding: 5px;">US, A, 3,472,738, PUBLISHED 14 OCTOBER 1969, FOSTER.</td> <td style="border: 1px solid black; text-align: center; vertical-align: top; padding: 5px;">1-31</td> </tr> <tr> <td style="border: 1px solid black; text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="border: 1px solid black; padding: 5px;">CA, A, 854,156, PUBLISHED 20 OCTOBER 1970, FOSTER.</td> <td style="border: 1px solid black; text-align: center; vertical-align: top; padding: 5px;">1-31</td> </tr> <tr> <td style="border: 1px solid black; text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="border: 1px solid black; padding: 5px;">N, CONTRACEPTION, ISSUED JUNE 1975, J.A. BLAIN ET AL, PEROXIDASE EN HUMAN CERVICAL MUCUS DURING THE MENSTRUAL CYCLE, PAGES 677-680.</td> <td style="border: 1px solid black; text-align: center; vertical-align: top; padding: 5px;">1-31</td> </tr> </table>			Category [*]	Citation of Document, ¹⁶ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No. ¹⁸	X	US, A, 3,472,738, PUBLISHED 14 OCTOBER 1969, FOSTER.	1-31	X	CA, A, 854,156, PUBLISHED 20 OCTOBER 1970, FOSTER.	1-31	X	N, CONTRACEPTION, ISSUED JUNE 1975, J.A. BLAIN ET AL, PEROXIDASE EN HUMAN CERVICAL MUCUS DURING THE MENSTRUAL CYCLE, PAGES 677-680.	1-31
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<div style="font-size: small;"> [*] Special categories of cited documents: ¹⁵ "A" document defining the general state of the art "E" earlier document but published on or after the international filing date "L" document cited for special reason other than those referred to in the other categories "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but on or after the priority date claimed "T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention "X" document of particular relevance </div>														
IV. CERTIFICATION <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; border-bottom: 1px solid black; padding: 5px;"> Date of the Actual Completion of the International Search ¹ 01 AUGUST 1980 </td> <td style="width: 50%; border-bottom: 1px solid black; padding: 5px;"> Date of Mailing of this International Search Report ² <div style="font-size: large; font-weight: bold; text-align: center;">13 AUG 1980</div> </td> </tr> <tr> <td style="border: 1px solid black; padding: 5px;"> International Searching Authority ¹ ISA/US </td> <td style="border: 1px solid black; padding: 5px;"> Signature of Authorized Officer ²⁰ ROBERT J. WARDEN </td> </tr> </table>			Date of the Actual Completion of the International Search ¹ 01 AUGUST 1980	Date of Mailing of this International Search Report ² <div style="font-size: large; font-weight: bold; text-align: center;">13 AUG 1980</div>	International Searching Authority ¹ ISA/US	Signature of Authorized Officer ²⁰ ROBERT J. WARDEN								
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(21) International Application Number: PCT/US80/00813 (22) International Filing Date: 20 June 1980 (20.06.80) (31) Priority Application Number: 050,810 (32) Priority Date: 21 June 1979 (21.06.79) (33) Priority Country: US (71) Applicants; and (72) Inventors: OSTER, Gerald [US/US]; 242 West 11th Street, New York, NY 10014 (US). KESTON, Albert, S. [US/US]; 67 Bonn Place, Weehawken, NJ 07087 (US). (74) Agent: BONNELL, Allan, H.; Brumbaugh, Graves, Donohue & Raymond, 30 Rockefeller Plaza, New York, NY 10012 (US).		(81) Designated States: AT (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), JP, LU (European patent), NL (European patent), SE (European patent). Published <i>With international search report Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: SPECIFIC IMPENDING OVULATION INDICATOR (57) Abstract Method for detecting impending ovulation in the human female by testing means employable by the average person. The test method involves contacting vaginal fluid samples with a bibulous mat containing an antibody against estrogen-induced peroxidase. The mat is then washed and tested for peroxidase.		

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DescriptionSpecific Impending Ovulation IndicatorTechnical Field

5 This invention relates to methods of detecting impending ovulation in human females, including methods which are sufficiently simple so that a woman can carry out the test on herself without the aid of a physician.

Background Art

10 While prior methods of fertility or ovulation testing have been proposed, prior tests have one or more undesirable aspects. For example, in the prior art the method of utilizing thermometry (the basal body temperature method) provides information on fertility, but this test merely indicates that ovulation has already occurred and does not detect impending ovulation.

15 The prior ovulation detection methods involving an examination of cervical mucus for its flow properties, saline content, glucose content and the like, are also deficient in that they do not easily lend themselves to self-examination by the woman and require sampling of the
20 posterior portion of the vagina. Similarly, microscopic examination of vaginal cells for staining characteristics and morphology require expensive apparatus and involve techniques which are usually beyond the skill of the average woman. Estrogen analysis of blood and urine is
25 likewise complicated and difficult to carry out.

Means for peroxidase testing have been known since 1898. Such means have been used for over 75 years for the detection of blood, including commercial articles sold, for example, by Smith Kline and French Laboratories
30 and by Miles Laboratories, for the detection of occult blood in urine and feces. Despite the long history



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of the peroxidase test it has not been previously used to determine the surge in estrogen-induced peroxidase in vaginal fluid for the detection of impending ovulation. This may be due to the fact that pathological conditions or injuries resulting in blood being present in the vagina contribute to a false positive indication for estrogen-induced peroxidase. It is known that hemoglobin and its degradation products exhibit a peroxidase-like reaction and, indeed, this property is utilized in the occult blood test for urine and feces.

Disclosure of Invention

In the approximately two to three days prior to ovulation in the menstrual cycle of normal human females there is a surge in the amount of estrogen-induced peroxidase (EIP) in the vaginal fluid. A simple form of the invention contemplates the woman taking a sample of vaginal fluid with, for example, a moistened cotton swab and contacting the swab with, for example, a bibulous mat containing an antibody against EIP. After contact of the swab with the mat, the mat is washed with water to remove interfering substances which do not combine with the antibody. An EIP-antibody combination possesses peroxidase activity, hence a positive peroxidase test on the aforesaid bibulous mat which had been in contact with a vaginal fluid sample and washed, indicates that EIP was present in the vaginal fluid. A negative test for peroxidase indicates the absence of EIP. If EIP is found, it indicates impending ovulation. An advantage of the present invention is that a specific antibody to EIP is used and this antibody combines only with EIP and not with the interfering substances. Chromogenic substrates of peroxidase and a hydroperoxide are used as a test for peroxidase.



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Best Mode For Carrying Out The Invention

5 A simple method for the detection of impending ovulation in women, as in the present invention, is of the highest importance to the human race and is of paramount interest to such prestigious organizations as the Population Council, the Ford Foundation, the National Institutes of Health and the World Health Organization. With the present invention a woman can, by herself, determine her impending fertile time. There is extensive
10 clinical evidence that for women the fertile time commences within 12 to 72 hours of ovulation (C. Tietze Fertility and Sterility, Vol. 11, p. 485, 1960). By abstaining from coitus or by otherwise protecting herself from insemination during the fertile time, a woman
15 can avoid pregnancy. Thus with the aid of the present invention, which enables a woman to determine her fertile time, this form of birth control could, if practiced widely, substantially reduce the rate of world population growth. Using the present invention one may practice
20 birth control without interference with the normal female hormonal function, such as occurs with the contraceptive pill which is objectionable to certain segments of the world population on religious grounds, as well as to others on medical grounds due to the possible serious
25 side effects. A woman practicing abstinence during the fertile period as determined by the present invention may avoid the need for contraceptive devices, such as the intrauterine device, for birth control which are considered undesirable to some.

30 The present invention may also be an aid to couples who wish to have a child, but have failed because of, for example, incorrect timing of coitus. Thus it may be seen that because the present invention can be a valuable aid in family planning, it serves an important humanitarian purpose.
35



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According to the present invention the woman moistens a cotton swab with vaginal fluid and then brings it into contact with a bibulous mat containing an antibody against EIP. The mat is then washed and tested for the presence
5 of peroxidase with a hydroperoxide and a chromogenic substrate of peroxidase.

The hydroperoxide may be hydrogen peroxide or a hydroperoxide generating system, such as the inorganic peroxides, sodium peroxide, barium peroxide, strontium
10 peroxide, sodium perborate, and the like, or organic hydroperoxides, such as methyl hydroperoxide or ethyl hydroperoxide. Many compounds, for example, sodium peroxide, barium peroxide, strontium peroxide, sodium perborate, and the bis (1-hydroxyalkyl) peroxides
15 generate hydrogen peroxide when moistened. Enzymatic reactions such as the action in air of L-amino oxidase on L-amino acids also generate hydrogen peroxide. The word hydroperoxide as used herein and in the claims is meant to include all of the compounds and types of com-
20 pounds of this type including the hydroperoxide generating compounds and enzyme systems which generate hydrogen peroxide.

A substance which becomes colored in the presence of peroxidase and a hydroperoxide is designated herein as a
25 chromogenic substrate of peroxidase or as a chromogen. Chromogenic peroxidase substrates or chromogens which may be employed in the present invention include the following substances:

- 30 1) Monoamines, such as aniline and its derivatives, orthotoluidine, para-toluidine, etc.;
- 2) Diamines, such as ortho-phenylenediamine, N,N dimethylpara-phenylenediamine, N,N diethyl-phenylenediamine, benzidine, 3,3',5,5', tetra-methyl benzidine, dianisidine, o-tolidine, etc.;



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- 3) Phenols, such as phenol per se, thymol, ortho, meta and para-cresols, alpha-naphthol, p,p-dihydroxybiphenyl, phloroglucinol and guaiacol;
- 4) Aromatic acids, such as salicylic, pyrocatechuic and gallic acids;
- 5) Leucodyes, such as leucomalachite green (to produce malachite green) and leucophenolphthalein (desirably employed in an alkaline medium);
- 6) Colored dyes, such as 2,6 dichlorophenol indophenol;
- 7) Various biological substances, such as epinephrine, the flavones, tyrosine, dihydrophenylalanine (producing an orange-reddish color) and tryptophane. Other substances such as gum guaiac, guaiaconic acid, Nadi reagent (producing a bluish color), bilirubin (producing a greenish color), iodides (which produce a brown color and, if starch is present, produce a deep blue color which is much stronger than iodide alone).

Some of the substances may be most effectively used in combination rather than individually. For example, Nadi reagent is such a mixture, namely naphthol and p-phenylenediamine, which gives a better final color than the individual components. Another example is a mixture of 4-amino antipyrine and 1,7-dihydroxynaphthalene.

Many of the chromogens, notably 3,3',5,5' tetramethyl benzidine, orthotolidine and p,p'-biphenol give a more intense color if halogen ions, such as iodide and bromide ions, or if halogenoid ions, such as thiocyanate and selenocyanate ions, are present.

One of the preferred chromogens of the invention comprises 3,3',5,5' tetramethyl benzidine and potassium



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thiocyanate; this mixture yields an intense blue color in a positive test. Another preferred chromogen is a mixture of p,p'-biphenol and potassium thiocyanate.

5 Substrates which change their fluorescence in the presence of a peroxidase and hydrogen peroxide include a loss of fluorescence of scopoletin or a production of fluorescence with, for example, dichlorofluorescein or homovanillic acid. Chemiluminescence is produced in the presence of peroxidases and hydrogen peroxide for
10 the following typical substances, Luminol, zinc tetraphenylporphyrine and the like.

Antibodies against human vaginal fluid EIP may be prepared by injecting rabbits with human vaginal fluid EIP purified according to the procedures described by
15 E. R. DeSombre and C.R. Lytle in Cancer Research, Volume 38, November 1978, pp. 4086-4099; but, instead of using rat mammary tumor extract, the said human vaginal fluid sample is used. The injections into rabbits take place at regular intervals together with
20 Freund's complete adjuvant in a manner well known to those skilled in immunology. After immunization to EIP has been achieved, antisera are collected. The antisera may be treated by methods well known to immunologist to obtain globulin samples which are enriched in
25 EIP antibodies. The term antibody as used herein and in the claims denotes pure antibody against EIP, purified antibody against EIP, solutions comprising antibody against EIP, mixtures comprising antibody against EIP, antisera against EIP and also includes antibody
30 against the apoenzyme of EIP. Not only will antibodies against EIP function in the invention, but also antibodies against the apoenzyme of EIP will function in this invention and should be understood to be included herein and in the claims.



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Instead of injecting rabbits in the aforestated procedure for preparing the antibody to EIP, the technique involving lymphocyte hybridomas may be employed. Lymphocyte hybridoma techniques are described in the

5 book entitled Lymphocyte Hybridomas published by Springer Verlag Berlin, Heidelberg: New York, 1978. The technique for making monoclonal antibodies by the technique of lymphocyte hybridomas is described in detail in the

10 chapter by M. M. Trucco, J. W. Stocker, and R. Ceppellini in the aforesaid book, where in place of human lymphoblastoid cells employed by the aforesaid workers, purified EIP from human vaginal fluid samples or the apoenzyme of it may be used. Monoclonal antibodies against different antigenic determinants in EIP or its apoenzyme

15 may be mixed to effect a precipitating antibody. Either monoclonal or mixed monoclonal antibodies may be employed in the present invention.

Some animals may produce species specific EIP which may be similar enough so that the antibodies to it may

20 cross-react with human vaginal fluid EIP. In such cases animal vaginal fluid EIP may be used to produce antibodies which may be used in place of the human antibody to EIP. Tissue cultures of human estrogen-sensitive tissue, such as human endometrium and the like, may produce the apoenzyme of EIP, in which case EIP apoenzyme

25 from such tissue cultures may be used as a source of apoenzyme which may be used in the present invention.

The apoenzyme of human EIP may be produced by the chemical synthesis of DNA and recombinant DNA methods

30 well known to those skilled in the art. Expression in E. Coli of chemically synthesized genes for human EIP or its apoenzyme may be carried out as described by D. V. Goeddel et al. in Proc. Nat. Acad. Sci. USA, Vol. 76,



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January 1979, pp. 106-110 where instead of human insulin one uses the aforesaid purified human EIP or its apo-enzyme.

5 A preferred embodiment of the present invention comprises antibody to EIP attached to a solid support. There are many methods well known to those skilled in the art of affixing an antibody to a bibulous mat or to the surface of other solid support materials such as wood, plastic, glass, ceramic and the like. Said solid support may be in the form of a film, spheres, beads, tubes, ion exchange materials (such as glass beads comprising arylamino groups or comprising carboxyl groups such as produced by Corning Glass Works), filter paper loaded with ion exchange resins (such as produced by 10 Whatman Paper Company), or paper loaded with Duolite ion exchange resin (the resin being made by Diamond Shamrock Company). With ion exchange resins the antibody is adsorbed but the antibody is not covalently linked. Antibody may be covalently linked to solid supports which 20 comprise aryl amino groups or which comprise carboxyl groups by methods well known in the art. For example, the aryl amino groups on solid supports may be diazotized with nitrous acid (sodium nitrite and freshly added hydrochloric acid), washed with water and then treated 25 with a solution comprising the antibody in sodium bicarbonate solution. Antibody may be coupled to carboxyl groups on solid supports by means of the carbodiimide reaction.

Example 1

30 Vaginal samples are taken daily starting on day 5 of a woman's menstrual cycle, where day 1 is taken as the day when menstruation began. Such vaginal samples can be obtained using a standard six inch cotton-tipped



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swab ("Puritan", Hardwood Products Co.). The cotton end can be moistened with water and rolled gently on the wall of the anterior vagina.

5 The swab, while still moist, is then contacted with a paper to which was affixed an antibody to estrogen-induced peroxidase. After contact for 10 to 30 minutes, the paper was washed in water. The still moist paper containing the antibody is pressed against starch-iodide test paper and the test paper is moistened with 10 0.01% hydrogen peroxide. A strong blue color is regarded as a positive test and weak or no coloration is regarded as a negative test.

For best results it is preferable to start on day 5 or day 6 for the daily routine. The first positive test 15 may be taken to indicate that ovulation is impending and will follow within two or three days.

In place of starch-iodide test paper, filter paper impregnated with 3,3',5,5' tetramethylbenzidine and potassium thiocyanate, impregnated with p,p' biphenol 20 and sodium thiocyanate, or guaiac, or orthotolidine or other chromogenic substrates may be used. The "Hemoccult" test of Smith Kline and French Laboratories, which according to the manufacturer consists of paper impregnated with orthotolidine, may also be used.

25 Example 2

In place of the cotton-tipped swab of Example 1, the vaginal fluid sample is obtained by directly contacting the vaginal wall with a piece of moist filter paper to which an antibody to estrogen-induced peroxidase was 30 attached. The filter paper was affixed toward the end of a plastic strip about 0.012 inches thick, 0.20 inches wide and 8 inches long and made of cellulose acetate.



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The paper is removed from the vagina after 20 minutes and was then washed with water. While still moist the paper is contacted with the occult blood detector part of the commercially available "Hemicombi-
5 stix" (Ames Company), which according to the manufacturer comprises orthotolidine and cumene hydroperoxide. A positive test (i.e., strong blue coloration) indicates impending ovulation.

10 In place of the occult blood detection part of "Hemicombistix", the occult blood peroxidase detector manufactured by Boehringer Company may be used, which detector, according to the manufacturer, contains ortho-
tolidine and dimethyl dihydroperoxy hexane.

15 In place of the above-mentioned peroxidase detectors, starch-iodide paper containing dry sodium perborate may be used.

Example 3

In place of the plastic strip in Example 2 in which the antibody to estrogen-induced peroxidase is toward
20 one end and a separate occult blood detector is provided on another strip, a strip was made with both the antibody and the blood detector as parts of the same strip, the antibody being at one end and the detector at the
25 other end. The contact between the two was achieved by folding the strip at its middle and holding the ends in contact after the antibody end had been contacted with the vagina and had been washed.

Example 4

30 A swab similar to that of Example 1 and containing vaginal fluid is dipped into a 1% solution of sodium chloride contained in a test tube. Affixed to the inner wall of the test tube. Affixed to the inner wall of the test tube is an antibody to estrogen-induced peroxidase. After 30 minutes the swab is



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removed from the test tube and the test tube is rinsed with water. Into the test tube is poured a solution containing 0.001% 3,3',5,5' tetramethylbenzidine to which had been freshly added 0.005% final concentration of hydrogen peroxide. A blue color is a positive indication of estrogen-induced peroxidase in the vaginal sample.

Example 5

A swab similar to that of Example 1 and containing vaginal fluid can be dipped into a solution containing 0.1 milligram per milliliter of rabbit antisera against estrogen-induced peroxidase. After 30 minutes activated charcoal is added. It is occasionally stirred, and the suspension is filtered. To the filtrate is added 0.001% final concentration of 3,3',5,5' tetramethylbenzidine and 0.1% final concentration potassium iodide, to which a 0.005% final concentration of hydrogen peroxide is freshly added. A blue color is a positive indication of estrogen-induced peroxidase in the vaginal sample.

Example 6

A swab similar to that of Example 1 and containing vaginal fluid can be dipped into a solution containing 0.01 milligram per milliliter of mixed clonal antibody to estrogen-induced peroxidase as described herein. The mixture is centrifuged and the supernatant is allowed to stand for 12 hours. The system is centrifuged again, the supernatant discarded, and the pellet was suspended with stirring into a 0.1% sodium chloride solution. After the system is again centrifuged, the pellet is contacted with starch-iodide paper and moistened with a 0.0005% hydrogen peroxide. A blue coloration is a positive indication of estrogen-induced peroxidase in the vaginal sample.



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Claims

1. An indicator for detecting impending ovulation comprising a substrate which includes an antibody against estrogen-induced peroxidase in vaginal
5 fluid samples and means for association therewith to detect estrogen-induced peroxidase immunoadsorbed by said antibody.
2. An indicator according to claim 1, wherein said means includes a chromogenic substrate of peroxidase.
10 dase.
3. An indicator according to claim 1, wherein said means includes a hydroperoxide.
4. An indicator according to claim 1, wherein said means includes a chromogenic substrate of peroxidase and a hydroperoxide.
15 dase and a hydroperoxide.
5. A claim according to claim 1, where said substrate is a solid support.
6. A claim according to claim 2 where said chromogenic substrate is on a solid support.
- 20 7. A claim according to claim 3 where said hydroperoxide is on a solid support.
8. A claim according to claim 4 where said hydroperoxide and said chromogenic substrate are on a solid support.
9. A claim according to claim 4 where said solid support is a bibulous mat.
25 is a bibulous mat.
10. A claim according to claim 5 where said solid support is a bibulous mat.
11. A claim according to claim 6 where said solid support is a bibulous mat.
- 30 12. A claim according to claim 7 where said solid support is a bibulous mat.



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13. A claim according to claim 2 where the chromogenic substrate of peroxidase is guaiac.
14. A claim according to claim 2 where the chromogenic substrate of peroxidase is bilirubin.
- 5 15. A claim according to claim 2 where the chromogenic substrate of peroxidase is starch and a soluble iodide salt.
16. A claim according to claim 2 where the chromogenic substrate of peroxidase is orthotolidine.
- 10 17. A claim according to claim 2 where the chromogenic substrate of peroxidase is p,p'biphenol and a soluble thiocyanate salt.
18. A claim according to claim 2 where the chromogenic substrate of peroxidase is 3,3',5,5'tetramethyl-
15 benzidine and a soluble bromide salt.
19. A claim according to claim 2 where the chromogenic substrate of peroxidase is 3,3',5,5' tetramethyl-
benzidine and a soluble iodide salt.
20. A claim according to claim 2 where the chromogenic
20 substrate of peroxidase is orthodianisidine and a soluble iodide salt.
21. A claim according to claim 3 where the said hydro-
peroxide is a substance which generates a hydro-
peroxide when moistened.
- 25 22. A claim according to claim 3 where said hydro-
peroxide is an enzyme-substrate system which
generates hydrogen peroxide.
23. An indicator according to claim 2 wherein the sub-
strate is a solid support which comprises in dif-
ferent regions of said support antibody against
30 estrogen-induced peroxidase from vaginal fluid,
a hydroperoxidase and a chromogenic substrate of
peroxide.



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24. An indicator according to claim 3 wherein the substrate is a solid support which comprises in different regions of said support antibody against estrogen-peroxidase from vaginal fluid and a hydroperoxide.
25. An indicator according to claim 2 wherein the substrate is a solid support which comprises in different regions of said support antibody against estrogen-induced peroxidase from vaginal fluid and a chromogenic substrate of peroxidase.
26. A method for producing antibodies against estrogen-induced peroxidase by injection of an animal with human vaginal fluid.
27. A method for producing antibodies against estrogen-induced peroxidase using in the lymphocyte hybridoma method human vaginal fluid.
28. A method for producing antibodies against estrogen-induced peroxidase by injection of an animal with an apoenzyme of estrogen-induced peroxide.
29. A method for producing antibodies against estrogen-induced peroxidase using in the lymphocyte hybridoma method an apoenzyme of estrogen-induced peroxidase.
30. A method for producing the apoenzyme of estrogen-induced peroxidase from tissue cultures of estrogen-sensitive tissue.
31. A method for producing the apoenzyme of estrogen-induced peroxidase from recombinant DNA methods.
32. A method for detecting impending ovulation in which a substrate which includes an antibody against estrogen-induced peroxidase is contacted with a vaginal fluid sample and then a test is performed for estrogen-induced peroxidase immunoadsorbed onto said substrate.

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33. A method according to claim 32 where said substrate is an inert solid support for said antibody.
34. A method according to claim 33 wherein said test for peroxidase comprises a chromogenic substrate for peroxidase and a hydroperoxide.
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INTERNATIONAL SEARCH REPORT

International Application No PCT/US80/00813

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) *		
According to International Patent Classification (IPC) or to both National Classification and IPC		
INT. CL. ⁹ A61K 39/00; C12Q 1/66, 1/28; G01N 33/48		
U.S. CL. 23/230B; 424/12,85; 435/7,28		
II. FIELDS SEARCHED		
Minimum Documentation Searched *		
Classification System	Classification Symbols	
U.S.	23/230B; 435/7,28,805; 424/12,85	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched *		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ¹⁴		
Category *	Citation of Document, ¹⁵ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No. ¹⁶
X	US, A, 3,817,837, PUBLISHED 18 JUNE 1974, RUBENSTEIN ET AL.	1-34
X	US, A, 4,070,492, PUBLISHED 24 JANUARY 1978, SPECTOR.	1-34
X	US, A, 3,472,738, PUBLISHED 14 OCTOBER 1969, FOSTER.	1-34
X	US, A, 3,644,177, PUBLISHED 22 FEBRUARY 1972, ZYK.	1-34
X	N, CONTRACEPTION, ISSUED JUNE 1975, J.A. BLAIN ET AL, PEROXIDASE IN HUMAN CERVICAL MUCUS DURING THE MENSTRUAL CYCLE, PAGES 677-680.	1-34
<p>* Special categories of cited documents: ¹⁸</p> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>"A" document defining the general state of the art</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document cited for special reason other than those referred to in the other categories</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> </div> <div style="width: 45%;"> <p>"P" document published prior to the international filing date but on or after the priority date claimed</p> <p>"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search :		Date of Mailing of this International Search Report :
08 OCTOBER 1980		14 OCT 1980
International Searching Authority :		Signature of Authorized Officer ¹⁹ :
ISA/US		ROBERT J. WARDEN